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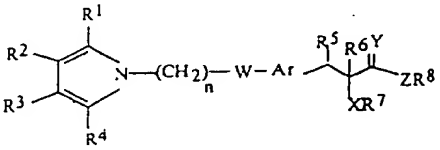
(54) Title: NOVEL COMPOUNDS HAVING HYPOLIPEDEMIC, HYPOCHOLESTEREMIC ACTIVITIES, PROCESS FOR THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM



(I)

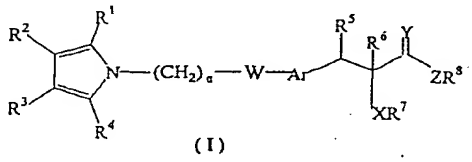
(57) Abstract: The present invention relates to novel substituted pyrrole compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them. This invention particularly relates to novel substituted pyrrole compounds of the general formula (I), their analogs, their derivatives, their polymorphs, their tautomeric forms, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and the pharmaceutical compositions containing them. This invention also relates to the process for preparing such compounds, a composition containing such a compound and the use of such a compound and composition in medicine.

WO 01/53257 A2

NOVEL COMPOUNDS HAVING HYPOLIPEDEMIC, HYPOCHOLESTEREMIC, ACTIVITIES, PORCESS FOR THEIR AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM

Field of Invention

The present invention relates to novel hypolipidemic and hypocholesterolemic compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them.



(I)

More particularly, the present invention relates to novel β-aryl-α-substituted propanoic acids of the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, pharmaceutically acceptable compositions containing them, their preparation, novel intermediates in their preparation and the use of these compounds in medicine.

The present invention also relates to a process for the preparation of the above said novel compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, novel intermediates and pharmaceutical compositions containing them.

The compounds of general formula (I) lower total cholesterol (TC), low-density lipoproteins (LDL), triglycerides and free fatty acids and increase high-density lipoproteins. The compounds of the general formula (I) are useful in the treatment of metabolic disorders categorized, as Syndrome X. The characteristic features of Syndrome X include initial insulin resistance leading to hyperinsulinemia, dyslipidemia and impaired glucose tolerance, which can further progress to non-insulin dependent diabetes mellitus (Type 2 diabetes), characterized by hyperglycemia which may lead to diabetic complications.

The compounds of the general formula (I) are useful in the treatment and/or prophylaxis of diseases such as obesity, hyperlipidemia, hyperglycemia especially type 2 diabetes, hypertension, cardiovascular diseases especially atherosclerosis. Also, the compounds of the general formula (I) are useful in treating renal diseases which may be associated with type 2 diabetes, for example, diabetic nephropathy, glomerulonephritis glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis and end stage renal diseases, for the prevention or retardation of the progression of microalbuminuria to albuminuria. The

compounds of the present invention are useful in the treatment and/or prophylaxis of psoriasis, polycystic ovarian syndrome, osteoporosis, inflammation and inflammatory bowel diseases, arteriosclerosis, xanthoma, pancreatic, myotonic dystrophy, disorders due to endothelial cell activation and hyperlipidemia. The compounds of the present invention are useful in the treatment of the above mentioned diseases in combination or along with one or more hypoglycemic, antihyperglycemic, hypolipidemic, hypolipoproteinemic agents such as statins, glitazones, sulfonyl urea's, fibric acid derivatives, α-glycosidase inhibitors or antioxidants and the like.

Background of the invention

The present invention relates to compounds represented by the general formula (I) having utility as hypocholesterolemic, hypolipidemic, hypolipoproteinemic, antiobesity and antihyperglycemic agents; methods for their preparation and methods for their use and pharmaceutical compositions containing them.

Hyperlipidemia has been recognized as the major risk factor in causing cardiovascular diseases due to atherosclerosis. Atherosclerosis and other such peripheral vascular diseases affect the quality of life of a large population in the world. During the treatment, emphasis is laid on lowering the elevated plasma cholesterol, low-density lipoprotein and plasma triglycerides as an important step to prevent occurrence of cardiovascular diseases. The details of etiology in atherosclerosis and coronary artery diseases is discussed by Ross and Glomset [New Engl. J. Med. 295, 369 - 377 (1976)]. Plasma cholesterol is generally esterified with various serum lipoproteins and numerous studies suggest an inverse relation between serum HDL-cholesterol concentration and cardiovascular disease. Numerous studies have indicated increased risk for occurrence of coronary artery diseases due to elevated LDL and VLDL-cholesterol levels [Stampfer *et al. N. Engl. J. Med.* 325, 373-381(1991)]. In other studies protective effects of HDL against progression of atherosclerosis are illustrated. Thus, HDL is a crucial factor in treating diseases with increased levels of cholesterol [Miller *et. al. Br. Med. J.* 282, 1741-1744(1981); Picardo *et al., Arteriosclerosis,* 6, 434-441 (1986); Macikinnon et *al., J. Biol. Chem.* 261, 2548-2552 (1986)].

Diabetes affects a large population and this condition is associated with a number of other complications. Usually, the disease is associated with other disease conditions such as obesity, hyperlipidemia, hypertension and angina. It is a well-recognized fact that improper treatment can aggravate impaired glucose tolerance and insulin resistance, leading to frank diabetes. Presently, sulfonamides and biguanides along with insulin are agents of choice in

treatment of diabetes. The limitations to this therapy include mild to severe hypoglycemia, which may lead to coma or in some cases may lead to death, which are mainly due to unsatisfactory glycaemic control. Recently, thiazolidinediones class of drugs having insulin-sensitizing action is being used in combination with other anti-diabetic agents, which includes troglitazone, rosiglitazone and pioglitazone. These are useful in the treatment of diabetes, and affect lipid metabolism. Patients with insulin resistance and type 2 diabetes often have raised triglycerides and low HDL-cholesterol concentrations and therefore, have greater risk of cardiovascular diseases. Thiazolidinediones are reported to have potential to induce tumor and are to cause hepatic dysfunction, which may lead to liver failure. Presently, there is need for safe and effective drug, to treat insulin resistance, diabetes and hyperlipidemia.

Obesity is another major health problem being associated with increased morbidity and mortality. It is a metabolic disorder, in which excess of fat is accumulated in the body. Although, the etiology of obesity is unclear, the general feature includes excess of calorie intake than that is consumed. Various therapies such as dieting, exercise, appetite suppression, inhibition of fat absorption etc. have been used to combat obesity. However, the need for more efficient therapies to treat this abnormality is essential as obesity is closely related to several diseases such as coronary heart disease, stroke, diabetes, gout, osteroarthritis, hyperlipidemia and reduced fertility. It also leads to social and psychological problems.

Peroxisome Proliferator Activated Receptor (PPAR) is a member of the steroid/ retinoid/ thyroid hormone receptor family. PPARα, PPARγ and PPARδ have been identified as subtypes of PPARs. PPARγ activation has been found to play a central role in initiating and regulating adipocyte differentiation [Endocrinology 135, 798-800, (1994)] and energy homeostasis, [Cell, 83, 803-812, (1995)]. During adipocyte differentiation, several highly specialized proteins are induced, which are being involved in lipid storage and metabolism. However, exact link from PPARγ activation to changes in glucose metabolism and decrease in insulin resistance in muscle has not been clear. PPARα is involved in stimulating β-oxidation of fatty acids [Trends Endocrine. Metabolism, 4, 291-296 (1993)] resulting in plasma circulating free fatty acid reduction [Current. Biol. 5, 618-621, 1995)]. Recently, role of PPARγ activation in the terminal differentiation of adipocyte precursors has been implicated in the treatment of cancer. [*Cell*, 79, 1147-1156 (1994); *Cell*, 79, 377-389 (1996); *Molecular Cell*, 465-470, (1998); *Carcinogenesis*, 1949-1953 (1998); *Proc. Natl. Acad. Sci.*,

94, 237-241 (1997); *Cancer Research*, 58, 3344-3352, (1998)]. Since PPARγ is expressed in certain cells consistently, PPARγ agonists would lead to nontoxic chemotherapy.

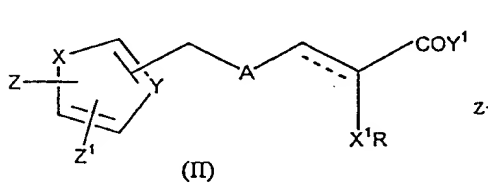
Leptin is a protein when bound to leptin receptors is involved in sending satiety signal to the hypothalamus. Leptin resistance would therefore lead to excess food in-take, reduced energy expenditure, obesity, impaired glucose tolerance and diabetes. It has been reported that insulin sensitizers lower plasma leptin concentration [*Proc. Natl. Acad. Sci.* 93,5793-5796, (1996): WO 98/02159)].

PPAR α agonists have been found useful in the treatment of obesity (WO 97/36579). Dual PPAR α and γ agonists have been suggested to be useful for Syndrome X (WO 97/25042). PPAR γ agonists and HMG-CoA reductase inhibitors have exhibited synergism and indicated the usefulness of the combination in the treatment of atherosclerosis and xanthoma (EP 0753 298).

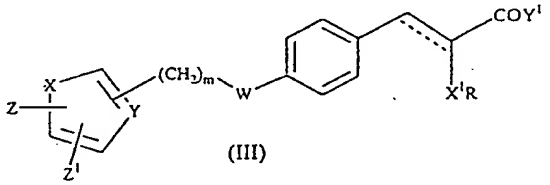
A number of compounds have been reported to be useful in the treatment of hyperlipidemia, hypercholesterolemia and hyperglycemia [US 5,306,726 US 5,985,884, US 6,054,453, EP 90 3343, PCT publications Nos. WO 91/19702, WO 94/01420, WO 94/13650, WO 95/03038, WO 95/17394, WO 96/04260, WO 96/04261, WO 96/33998, WO 97/25042, WO 97/36579, WO 98/28534, WO 99/08501, WO 99/16758, WO 99/19313, WO99/20614, WO 00/23417, WO 00/23445, WO 00/23451].

A few β-aryl-α-hydroxypropanoic acids, their derivatives, and their analogs have been reported to be useful in the treatment of hyperglycemia and hypercholesterolemia. Some of such compounds described in the prior art are outlined below :

1. U. S. patent 5,306,726 and WO 91/19702 disclose several 3-aryl-2-hydroxypropionic acid derivatives of general formulae (II) and (III) as hypolipidemic and hypoglycemic agents. Examples of these compounds are shown in the formulae (IV) and (V).



(II)



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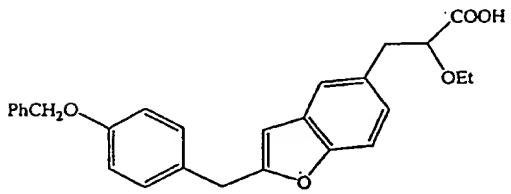
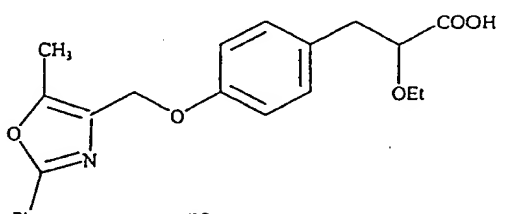
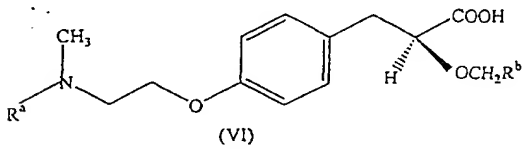


(IV)



(V)

2. International patent applications, WO 95/03038 and WO 96/04260 disclose compounds of formula (VI) wherein, R^a represents 2-benzoxazolyl or 2-pyridyl and R^b represent CF_3, CH_2OCH_3 or CH_3. A typical example is (S)-3-[4-[2-[N-(2-benzoxazolyl)N-methylamino]ethoxy]phenyl]-2-(2,2,2-trifluoroethoxy)propanoic acid (VII).



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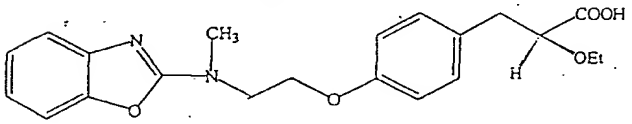
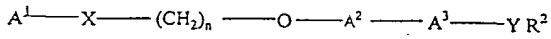


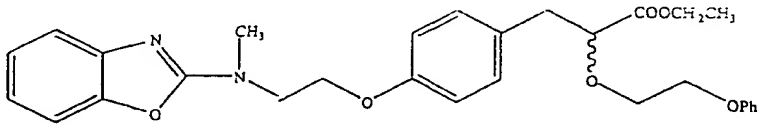
(VII)

3. International patent applications, WO 94/13650 and WO 94/01420 and WO/95/17394 disclose the compounds of general formula (VIII) wherein,



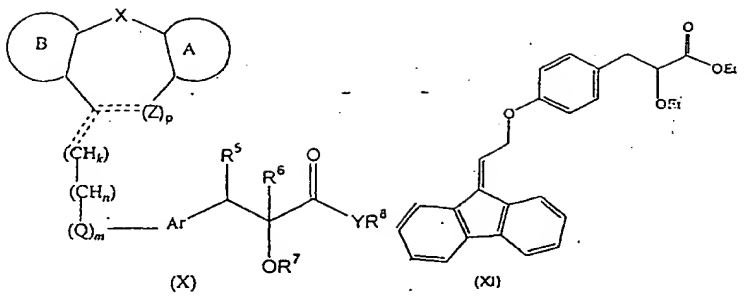
(VIII)

A^1 represents aromatic heterocycle moiety, A^2 represents substituted benzene ring and A^3 represents moiety of formula $(CH_2)_m$-CH-(OR^1), wherein R^1 represents alkyl groups, m is integer of 1-5; X represents substituted or unsubstituted N; Y represents C=O or C=S, R^2 represents OR^3 where R^3 may be hydrogen, alkyl, aralkyl, or aryl group and n is integer of 2-6. An example of these compounds is shown in formula (IX).

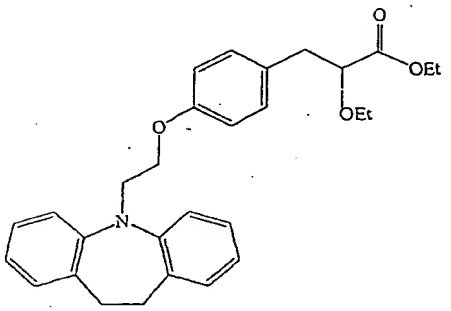


(IX)

4. International patent application, WO 00/23,445, WO 00/23,417 and WO 00/23,451 disclose cyclic compounds of the formula (X) useful in treatment of diabetes and obesity. A typical example of these compounds is shown formulae (XI) and (XII).

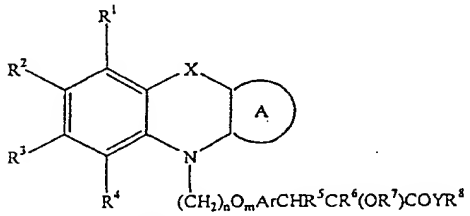


(X) (XI)



(XII)

5. WO 00/540,414, WO 99/16,758, WO 99/19,313 report compounds of general formula (XIII), (XIV), (XV) and (XVI) which reduce glucose, cholesterol and triglycerides.



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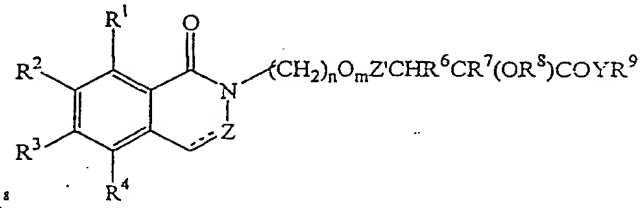

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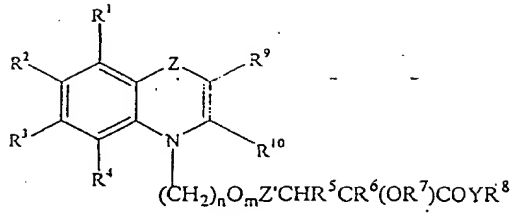

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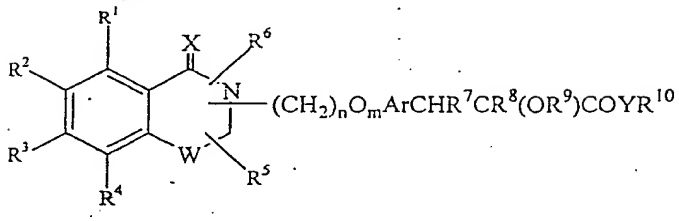


(XIV)

Summary of the Invention

The objective of this invention is to develop novel compounds represented by the general formula (I) having utility as hypocholesterolemic, hypolipidemic, hypolipoproteinemic, anti-obesity and antihyperglycemic agents which may have additional body weight lowering effect and beneficial effect in treatment and/or prophylaxis of diseases caused by hyperlipidemia, coronary artery diseases, diseases classified under syndrome X and atherosclerosis.

The main objective of the present invention is to provide novel β-aryl-α-substituted propanoic acids represented by the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, and pharmaceutical compositions containing them or their mixtures.

Another objective of the present invention is to provide novel β-aryl-α-substituted propanoic acids represented by the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, and pharmaceutical compositions containing them or their mixtures having enhanced activities, without toxic effects or with reduced toxic effect.

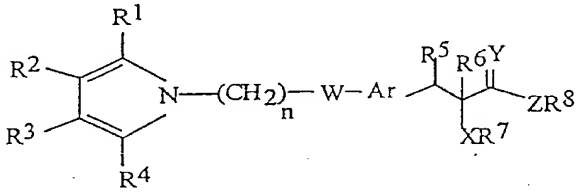
Yet another objective of this invention is to provide a process for the preparation of novel β-aryl-α-substituted propanoic acids represented by the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates.

Still another objective of the present invention is to provide pharmaceutical compositions containing compounds of the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates or their mixtures in combination with suitable carriers, solvents, diluents and other media normally employed in preparing such compositions.

A further objective of the present invention is to provide novel intermediates and a process for their preparation.

Detailed Description of the Invention

Accordingly, the present invention relates to compounds of the general formula (I).



(I)

wherein one or more groups R^1, R^2 R^3, R^4 may be same or different and represent hydrogen, halogen, perhaloalkyl, hydroxy, thio, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12})alkyl, (C_2-C_{12})alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C_1-C_{12})alkoxy, cyclo(C_3-C_7)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocycloalkoxycarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acid and its derivatives, phosphonic acid and its derivatives; or the adjacent groups R^2 and R^3 together may form a five or a six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from O, N, or S; n is an integer ranging from 1 to 8; W represents O, S or NR^9 where R^9 represents alkyl or aryl; Ar represents a substituted or unsubstituted divalent single or fused aromatic, heteroaromatic or heterocyclic group; R^5 and R^6 represent both hydrogen or together represent a bond; R^5 and R^6 may also represent a hydroxy, alkyl, alkoxy, halogen, acyl, substituted or unsubstituted

aralkyl group; X represents O or S; R^7 represents hydrogen, perfluoroalkyl, substituted or unsubstituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, alkoxyalkyl, aryloxyalkyl, alkoxycarbonyl, aryloxycarbonyl, cycloalkyloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl groups; Y represents O or S; Z represents oxygen or NR^{10}, where R^{10} represents hydrogen or substituted or unsubstituted groups selected from alkyl, aryl, aralkyl, hydroxyalkyl, aminoalkyl, heteroaryl, heteroaralkyl groups; R^8 represents hydrogen, substituted or unsubstituted groups selected from alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, alkoxyalkyl, alkylaminoalkyl groups; R^{10} and R^8 together may form a 5 or 6 membered substituted or unsubstituted cyclic ring structure containing carbon atoms or containing one or more heteroatoms selected from O, N and S.

Suitable groups represented by R^1, R^2, R^3 and R^4 may be selected from hydrogen, halogen atom such as fluorine, chlorine, bromine or iodine; perhaloalkyl particularly, perhalo(C_1-C_6)alkyl such as fluoromethyl, difluoromethyl, trifluoromethyl, trifluoroethyl, fluoroethyl, difluoroethyl and the like; hydroxy, thio, amino, nitro, cyano, formyl, amidino, guanidino groups; substituted or unsubstituted (C_1-C_{12}) alkyl group, especially, linear or branched (C_1-C_8)alkyl group, such as methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *t*-butyl, *n*-pentyl, *iso*-pentyl, hexyl, *iso*-hexyl, heptyl, octyl and the like; cyclo(C_3-C_7)alkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, the cycloalkyl group may be substituted; cyclo(C_3-C_7)alkenyl group such as cyclopentenyl, cyclohexenyl, cycloheptenyl, cycloheptadienyl, cycloheptatrienyl and the like, the cycloalkenyl group may be substituted; (C_1-C_{12})alkoxy, especially, (C_1-C_6)alkoxy group such as methoxy, ethoxy, propyloxy, butyloxy, *iso*-propyloxy and the like, which may be substituted; cyclo(C_3-C_7)alkoxy group such as cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy and the like, the cycloalkoxy group may be substituted; aryl group such as phenyl or naphthyl, the aryl group may be substituted; aryloxy group such as phenoxy, naphthyloxy, the aryloxy group may be substituted; aralkyl group such as benzyl, phenethyl, $C_6H_5CH_2CH_2CH_2$, naphthylmethyl and the like, the aralkyl group may be substituted and the substituted aralkyl is a group such as $CH_3C_6H_4CH_2$, Hal-$C_6H_4CH_2$, $CH_3OC_6H_4CH_2$, $CH_3OC_6H_4CH_2CH_2$ and the like; aralkoxy group such as benzyloxy, phenethyloxy, naphthylmethyloxy, phenylpropyloxy and the like, the aralkoxy group may be substituted; heterocyclyl groups such as aziridinyl, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl and the like, the heterocyclyl group may be substituted; heteroaryl group such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, tetrazolyl, benzopyranyl,

benzofuranyl and the like, the heteroaryl group may be substituted; heterocyclo(C_1-C_6)alkyl, such as pyrrolidinealkyl, piperidinealkyl, morpholinealkyl, thiomorpholinealkyl, oxazolinealkyl and the like, the heterocyclo(C_1-C_6)alkyl group may be substituted; heteroaralkyl group such as furanmethyl, pyridinemethyl, oxazolemethyl, oxazolethyl and the like, the heteroaralkyl group may be substituted; heteroaryloxy, heteroaralkoxy, heteroocycloalkoxy, heterocyclylalkoxy wherein heteroaryl, heteroaralkyl, heterocycloalkyl and heterocyclylalkyl moieties are as defined earlier and may be substituted; acyl group such as acetyl, propionyl or benzoyl, the acyl group may be substituted; acyloxy group such as MeCOO, EtCOO, PhCOO and the like which may optionally be substituted; acylamino groups such as CH_3CONH, C_2H_5CONH, C_3H_7CONH, C_6H_5CONH which may be substituted; (C_1-C_6)monoalkylamino group such as CH_3NH, C_2H_5NH, C_3H_7NH, $C_6H_{13}NH$ and the like, which may be substituted; (C_1-C_6)dialkylamino group such as $N(CH_3)_2$, $CH_3(C_2H_5)N$ and the like, which may be substituted; arylamino group such as C_6H_5HN, $CH_3(C_6H_5)N$, $C_6H_4(CH_3)NH$, NHC_6H_4-Hal and the like, which may be substituted; aralkylamino group such as $C_6H_5CH_2NH$, $C_6H_5CH_2CH_2NH$, $C_6H_5CH_2NCH_3$ and the like, which may be substituted; hydroxy(C_1-C_6)alkyl which may be substituted; amino(C_1-C_6)alkyl which may be substituted; mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl group which may be substituted; alkoxyalkyl group such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl and the like, which may be substituted; aryloxyalkyl group such as $C_6H_5OCH_2$, $C_6H_5OCH_2CH_2$, naphthyloxymethyl and the like, which may be substituted; aralkoxyalkyl group such as $C_6H_5CH_2OCH_2$, $C_6H_5CH_2OCH_2CH_2$ and the like, which may be substituted; (C_1-C_6)alkylthio, thio(C_1-C_6)alkyl which may be substituted; alkoxycarbonylamino group such as C_2H_5OCONH, CH_3OCONH and the like which may be substituted; aryloxycarbonylamino group such as C_6H_5OCONH, $C_6H_5OCONCH_3$, $C_6H_5OCONC_2H_5$, $C_6H_4CH_3OCONH$, $C_6H_4(OCH_3)OCONH$ and the like which may be substituted; aralkoxycarbonylamino group such as $C_6H_5CH_2OCONH$, $C_6H_5CH_2CH_2OCONH$, $C_6H_5CH_2OCON(CH_3)$, $C_6H_5CH_2OCON(C_2H_5)$, $C_6H_4CH_3CH_2OCONH$, $C_6H_4OCH_3CH_2OCONH$ and the like, which may be substituted; aminocarbonylamino group; (C_1-C_6)alkylaminocarbonylamino group, di(C_1-C_6)alkylaminocarbonylamino group, (C_1-C_6)alkylamidino group, (C_1-C_6)alkylguanidino, di(C_1-C_6)alkylguanidinogroups, hydrazino and hydroxylamino groups; carboxylic acid or its derivatives such as amides, like $CONH_2$, alkylaminocarbonyl like MeNHCO, Me_2NCO, EtNHCO, Et_2NCO, arylaminocarbonyl like PhNHCO, NapthNHCO and the like, aralkylaminocarbonyl such as $PhCH_2NHCO$, $PhCH_2CH_2NHCO$ and the like, heteroarylaminocarbonyl and heteroaralkylamino carbonyl groups where the heteroaryl groups are as defined earlier, heterocyclylaminocarbonyl where

the heterocyclyl group is as defined earlier; carboxylic acid derivatives such as esters, wherein the ester moieties are alkoxycarbonyl such as methoxycarbonyl or ethoxycarbonyl, which may be substituted; aryloxycarbonyl group such as unsubstituted or substituted phenoxycarbonyl, naphthyloxycarbonyl and the like; aralkoxycarbonyl group such as benzyloxycarbonyl, phenethyloxycarbonyl, naphthylmethoxycarbonyl and the like, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, wherein the heteroaryl group is as defined earlier, heterocycloxycarbonyl where heterocycle is as defined earlier and these carboxylic acid derivatives may be substituted; sulfonic acid or its derivatives such as SO_2NH_2, SO_2NHMe, SO_2NMe_2, SO_2NHCF_3, $SO_2NHCO(C_1\text{-}C_6)$alkyl, SO_2NHCOaryl where the aryl group is as defined earlier and the sulfonic acid derivatives may be substituted; phosphonic acid and its derivatives such as $P(O)(OH)_2$, $P(O)(O\ C_1\text{-}C_6\ alkyl)_2$, $P(O)(O\ aryl)_2$ and the like.

When the groups represented by R^1, R^2, R^3 and R^4 are substituted, the substituents are selected from halogen, hydroxy, nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, aralkoxy, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives or phosphonic acid or its derivatives.

Preferably the substituents on the pyrrole namely, R^1 to R^4 represent halogen atom such as fluorine, chlorine, bromine; hydroxy group, optionally halogenated groups selected from alkyl group such as methyl, ethyl, *n*-propyl, *iso*-propyl or *n*-butyl; cycloalkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl which may be substituted ; aryl group such as phenyl which may be substituted; aralkyl group such as benzyl which may be substituted; $(C_1\text{-}C_3)$alkoxy, benzyloxy, acyl or acyloxy groups; heterorayl such as thienyl, pyrrolyl, furyl, pyridyl, pyrimidinyl, imidazolyl, indolyl, oxazolyl, groups which may be substituted; carboxylic acid and its derivatives.

Suitable cyclic structures formed by the two adjacent groups R^2 and R^3 together with the carbon atoms to which they are attached contain 5 to 6 ring atoms which may optionally contain one or more heteroatoms selected from oxygen, nitrogen or sulfur and optionally contain one or more double bonds. The cyclic structure may be optionally substituted phenyl, pyridyl, furanyl, thienyl, pyrrolyl, imidazolyl, pyrimidinyl, pyrazinyl and the like. Suitable substituents on the cyclic structure formed by R^2 and R^3 together with the adjacent carbon atoms to which they are attached include oxo, hydroxy, halogen atom such as chlorine, bromine and iodine; nitro, cyano, amino, formyl, $(C_1\text{-}C_3)$alkyl, $(C_1\text{-}C_3)$alkoxy, thioalkyl, alkylthio phenyl or benzyl groups.

n is an integer ranging from 1-8. It is preferred that n be 1 to 4.

Suitable groups represented by Ar include substituted or unsubstituted groups selected from divalent phenylene, naphthylene, pyridyl, quinolinyl, benzofuryl, dihydrobenzofuryl, benzopyranyl, indolyl, indolinyl, azaindolyl, azaindolinyl, pyrazolyl, benzothiazolyl, benzoxazolyl and the like. The substituents on the group represented by Ar may be selected from substituted or unsubstituted linear or branched (C_1-C_6)alkyl, (C_1-C_3)alkoxy, halogen, haloalkyl, haloalkoxy, acyl, amino, acylamino, thio or carboxylic or sulfonic acids and their derivatives or phosphonic acid and their derivatives.

It is preferred that Ar represents substituted or unsubstituted divalent phenylene, naphthylene, benzofuryl, indolyl, indolinyl, quinolinyl, azaindolyl, azaindolinyl, benzothiazolyl or benzoxazolyl groups.

It is more preferred that Ar is represented by divalent phenylene or naphthylene, which may be unsubstituted or substituted by halogen, methyl, halomethyl, methoxy or halomethoxy groups.

Suitable R^5 includes hydrogen, lower alkyl groups such as methyl, ethyl or propyl; hydroxy, (C_1-C_3)alkoxy, halogen atom such as fluorine, chlorine, bromine, or iodine; aralkyl such as benzyl, phenethyl, which may be unsubstituted or substituted or R^5 together with R^6 represent a bond.

Suitable R^6 may be hydrogen, lower alkyl groups such as methyl, ethyl or propyl; hydroxy, (C_1-C_3)alkoxy; halogen atom such as fluorine, chlorine, bromine, iodine; acyl group such as linear or branched (C_2-C_{10}) acyl group such as acetyl, propanoyl, butanoyl, pentanoyl, benzoyl and the like; aralkyl such as benzyl, phenethyl, which may be unsubstituted or substituted or together with R^5 forms a bond.

When R^5 or R^6 represent substituted aralkyl, the preferred substitutents are hydroxy, halogen, alkyl and alkoxy.

It is preferred that R^5 or R^6 represent hydrogen atom or R^5 and R^6 together represent a bond.

Suitable groups represented by R^7 may be selected from hydrogen, substituted or unsubstituted, linear or branched (C_1-C_{16})alkyl, preferably (C_1-C_{12})alkyl group such as methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, pentyl, hexyl, octyl and the like; (C_3-C_7)cycloalkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like, the cycloalkyl group may be substituted; aryl group such as phenyl, naphthyl, the aryl group

may be substituted; heteroaryl group such as pyridyl, thienyl, furyl and the like, the heteroaryl group may be substituted; heteroaralkyl group such as furanemethyl pyridinemethyl, oxazolemethyl, oxazolethyl and the like, the heteroaralkyl group may be substituted; aralkyl group wherein the alkyl moiety may contain C_1-C_6 atoms such as benzyl and phenethyl etc, wherein the aryl moiety may be substituted; heterocyclyl group such as aziridinyl, pyrrolidinyl, piperidinyl and the like, the heterocyclyl group may be substituted; (C_1-C_6)alkoxy(C_1-C_6)alkyl group such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxypropyl and the like, the alkoxyalkyl group may be substituted; substituted or unsubstituted, linear or branched (C_2-C_{16})acyl group such as acetyl, propanoyl, butanoyl, benzoyl, octanoyl, decanoyl and the like; (C_1-C_6)alkoxycarbonyl, the alkyl group may be substituted; aryloxycarbonyl such as phenoxycarbonyl, naphthyloxycarbonyl, the aryl group may be substituted; (C_1-C_6)alkylaminocarbonyl, the alkyl group may be substituted; arylaminocarbonyl such as PhNHCO, or naphthylaminocarbonyl, the aryl moiety may be substituted. The substituents may be selected from the group consisting of halogen, hydroxy, nitro, or unsubstituted/substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, alkoxycarbonyl, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives.

Suitable groups represented by R^8 may be selected from hydrogen, substituted or unsubstituted, linear or branched (C_1-C_{16})alkyl, preferably (C_1-C_{12})alkyl group such as methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, pentyl, hexyl, octyl and the like; (C_3-C_7)cycloalkyl such as cyclopropyl, cyclopentyl, cyclohexyl and the like, the cycloalkyl group may be substituted; aryl group such as phenyl, naphthyl, the aryl group may be substituted; heteroaryl group such as pyridyl, thienyl, furyl and the like, the heteroaryl group may be substituted; heteroaralkyl group such as furanemethyl, pyridinemethyl, oxazolemethyl, oxazolethyl and the like, the heteroaralkyl group may be substituted; aralkyl group such as benzyl and phenethyl, the aralkyl group may be substituted; heterocyclyl group such as aziridinyl, pyrrolidinyl, piperidinyl and the like, the heterocyclyl group may be substituted. The substituents on R^8 may be selected from halogen, hydroxy, nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl aryloxy, aralkoxy, alkoxycarbonyl, alkylamino,

alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives.

Z represents oxygen or NR^{10}.

Suitable groups represented by R^{10} may be selected from hydrogen, substituted or unsubstituted, linear or branched (C_1-C_{16})alkyl, preferably (C_1-C_{12})alkyl; hydroxy(C_1-C_6)alkyl; aryl group such as phenyl, naphthyl; aralkyl group such as benzyl and phenethyl; heterocyclyl group such as aziridinyl, pyrrolidinyl, piperidinyl, and the like; heteroaryl group such as pyridyl, thienyl, furyl and the like; or heteroaralkyl group such as furanemethyl, pyridinemethyl, oxazolemethyl, oxazolethyl and the like.

The cyclic structure formed by R^8 and R^{10} together with the carbon atoms to which they are attached may be a substituted or unsubstituted 5 or 6 membered cyclic structure containing carbon atoms which may optionally contain one or two heteroatoms selected from oxygen, nitrogen or sulfur. The cyclic structure may contain one or more double bonds.

Suitable ring structures formed by R^8 and R^{10} together may be selected from pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, oxazolinyl, diazolinyl and the like. Suitable substituents on the cyclic structure formed by R^8 and R^{10} taken together may be selected from halogen, hydroxy, alkyl, oxo, aralkyl and the like.

For any R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10} and Ar that may be substituted, the substituents are as defined anywhere in this specification.

Suitable n is an integer ranging from 1 to 6, preferably n represents an integer 2 to 4.

Pharmaceutically acceptable salts forming part of this invention are intended to define but not limited to salts of the carboxylic acid moiety such as alkali metal salts like Li, Na, and K salts; alkaline earth metal salts like Ca and Mg salts; salts of organic bases such as lysine, arginine, guanidine, diethanolamine, choline, tromethamine and the like; ammonium or substituted ammonium salts and aluminum salts. Salts may be acid addition salts which defines but not limited to sulfates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulfonates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates and the like. Pharmaceutically acceptable solvates may be hydrates or comprising other solvents of crystallization such as alcohols.

Particularly useful compounds according to the present invention includes:

(±) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(+) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(-) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(±) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(+) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(-) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(±) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(+) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(-) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxyropanoate

(±) Ethyl 3-[4-[2-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl-2-ethoxypropanoate

(+) Ethyl 3-[4-[2-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl-2-ethoxypropanoate

(-) Ethyl 3-[4-[2-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl-2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl)-2-ethoxypropanoate

(-) Ethyl 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl)-2-ethoxypropanoate

(±) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanate

(+) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanate

(-) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanate

(±) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+)Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-(2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-(2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-(2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-(2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) Ethyl 3-[4-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl]- 2-ethoxypropanoic and its pharmaceutically acceptable salts

(+) Ethyl 3-[4-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl]- 2-ethoxypropanoic and its pharmaceutically acceptable salts

(-) Ethyl 3-[4-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl]- 2-ethoxypropanoic and its pharmaceutically acceptable salts

(±) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salt thereof

(+) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(±) 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl) -2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(+) 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl) -2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(-) 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl) -2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts.

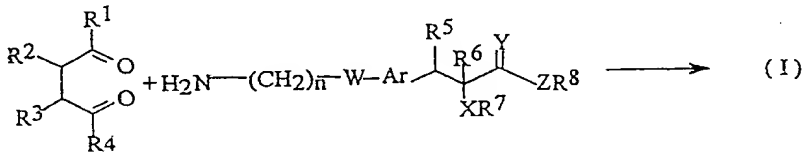
(±) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic and its pharmaceutically acceptable salts

(+) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic and its pharmaceutically acceptable salts

The present invention provides process for the preparation of novel compounds of this invention of the general formula (I), their tautomeric forms, their derivatives, their analogs, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts and their pharmaceutically acceptable solvates wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, W, X, Y, Z, Ar and n are as defined previously can be prepared by any of the methods described below:

Route 1:

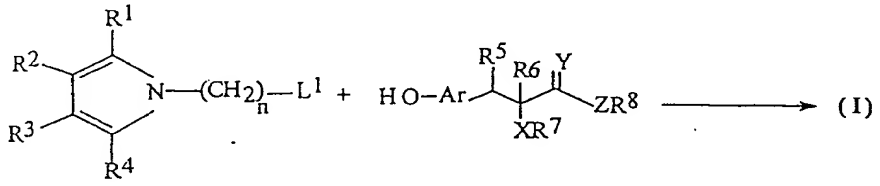


(1a) (1b)

The reaction of a compound of general formula (1a), wherein all symbols are as defined earlier with a compound of formula (1b) which may be chiral or racemic, wherein all symbols are as defined earlier to yield a compound of general formula (I) wherein all symbols are as defined earlier using Paal-Knorr cyclization (Paal C. Ber., 1885, 18, 367; Knorr, L., Ber., 1885, 18, 299). The reaction may be carried out neat or in the presence of a solvent or a mixture thereof such as tetrahydrofuran, hexane, toluene, ethanol, heptane, petroleum ether, xylene, benzene, ethyl acetate, tert-butyl acetate, 1,2-dichloroethane, *iso*-propanol, dioxane, cyclohexane and the like. The reaction temperature may range from 0 °C to the reflux temperature of the solvent(s) used. The water produced may be removed by using a Dean Stark water separator or by water scavengers such as molecular sieves. The reaction may be carried out in the presence of an inert atmosphere such as N_2, He or Ar. The reaction may be carried out in the presence of an acid, such as acetic acid, propanoic acid, butyric acid, isobutyric acid, pivalic acid, *p*-toluenesulfonic acid, camphorsulfonic acid, benzenesulfonic

acid, trifluoroacetic acid, chloroacetic acid, chloropropanoic acid, phenylacetic acid, phenylpropanoic acid, malonic acid, succinic acid, benzoic acid, halogenated benzoic acid, toluic acid and the like. Mineral acids such as HCl or HBr may also be used. The reaction time may range from 5 minutes to 72 hours, preferably from 1 to 48 hours.

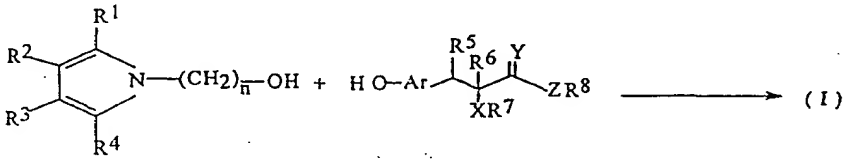
Route 2 :



(1c) (1d)

The reaction of compound of formula (1c), wherein all the symbols are as defined earlier and L^1 represents a leaving group such as halogen atom, *p*-toluenesulfonate, methanesulfonate, trifluoromethanesulfonate and the like with a compound of formula (1d) which may be chiral or racemic, wherein all the symbols are as defined earlier to produce a compound of general formula (I), wherein all the symbols are as defined earlier, may be carried out in the presence of solvents such as acetone, THF, DMSO, dioxane, DMF, DME and the like or a mixture thereof. Bases such as alkali metal carbonates such as K_2CO_3, Na_2CO_3, alkali metal hydrides such as NaH, KH may be used. The reaction may be carried out at a temperature in the range 0 °C to 150 °C and the reaction time may range from 1 to 48 hours.

Route 3 :

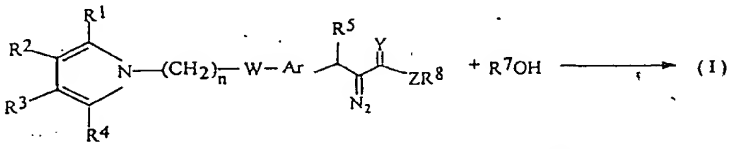


(1e) (1d)

The reaction of compound of general formula (1e) where all symbols are as defined earlier with a compound of general formula (1d) which may be chiral or racemic, defined earlier may be carried out using coupling agents such as DCC, EDC, triaryl phosphine/dialkyl azadicarboxylate such as PPh_3/DEAD or PPh_3/DIAD and the like. Inert atmosphere may be maintained using N_2, Ar or He. Solvents such as THF, Dioxane, DME, toluene, CH_2Cl_2, $CHCl_3$ CCl_4, acetonitrile and the like may be used. Compounds such as DMAP, HOBT may be used in the range of 0.05 to 2 equivalents. The reaction temperature in the range of 0 °C to

reflux temperature of the solvent may be used, preferably, 20 °C to 80 °C. The duration of the reaction may range from 0.5 to 24 h, preferably 0.5 to 12 hours.

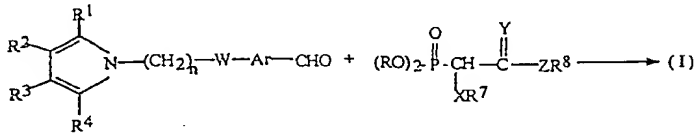
Route 4:



(1f) (1g)

The reaction of a compound of formula (1f) where all symbols are as defined earlier with an alcohol of formula (1g) where R^7 is as defined earlier except H, to produce a compound of formula (I) where all symbols are as defined earlier and X represents O atom, may be carried out in the presence of rhodium salts such as rhodium (II) acetate. Solvents such as benzene, toluene, ether, THF, dioxane and the like may be used. R^7OH may also be used as solvent to enhance the rate of the reaction. Inert atmosphere may be maintained using N_2, Ar or He. The reaction time may range from 0.25 to 48 hours, preferably 0.25 h to 8 h.

Route 5:



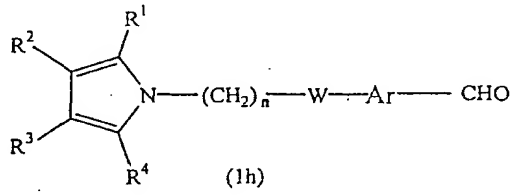
(1h) (1i)

The reaction of a compound of general formula (1h) wherein all the symbols are as defined earlier, with a compound of formula (1i), where all the symbols are as defined earlier and R represents (C_1-C_8) alkyl to afford a compound of formula (I) where R^5 and R^6 represent a bond and all other symbols are as defined earlier, may be carried out under Wittig Horner reaction conditions in the presence of a base such as alkali metal hydrides, like NaH or KI, alkali metal alkoxides such as NaOMe, NaOEt, K^+ t-BuO^- or mixture thereof, organolithiums like CH_3Li, BuLi, *sec*-BuLi, LDA and the like. Aprotic solvents such as THF, dioxane, DMF, DMSO, DME and the like or mixture thereof may be employed. HMPA favours the progression of the reaction but not essential. The reaction may be carried out at a temperature ranging from -80 °C to 50 °C, preferably, from 0 °C to 30 °C. The reaction proceeds more effectively under anhydrous conditions.

The compound of formula (I) where R^5 and R^6 represent a bond may be reduced to a compound of general formula (I) where R^5 and R^6 each represent hydrogen atom by reacting

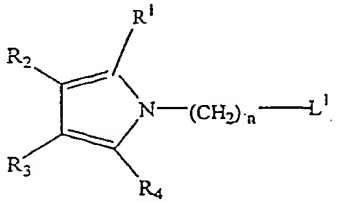
with hydrogen gas in the presence of a catalyst such as 5-10 % Pd/C, Rh/C, Pt/C Raney Ni and the like or 5-100 % w/w of the above mixture thereof catalyst may be employed. The pressure of hydrogen gas may be one atmosphere to 80 psi. Suitable solvents are alcohols such as ethanol, methanol and the like, ethyl acetate, acetic acid and the like. Metal-solvent such as magnesium in alcohol or sodium amalgam in alcohol may also be used.

According to a feature of the present invention, there is provided an intermediate of formula (1h) wherein R^1, R^2, R^3, R^4, W, n and Ar are as defined earlier.

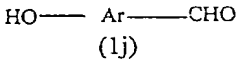


(1h)

According to another feature of the present invention, there is provided a process for the preparation of novel intermediate of the general formula (1h) as defined earlier which comprises reacting a compound of general formula (1c),



(1c)

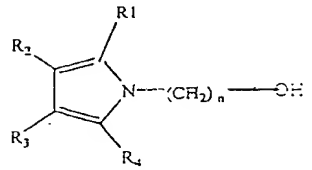


(1j)

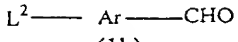
wherein, $R^1 - R^4$, n are as defined earlier and L^1 is a halogen atom such as chlorine, bromine or iodine or a leaving group such as methanesulfonate, trifluoromethanesulfonate, p-toluenesulfonate and the like with the compound of the formula (1j), where Ar is as defined earlier.

The reaction of the compound of formula (1c) with the compound of formula (1j) to produce a compound of formula (1h) may be carried out in the presence of solvents such as THF, DMF, DMSO, DME and the like. Mixture of solvents may be used. The inert atmosphere may be maintained by using inert gases such as N_2, Ar or He. The reaction may be effected in the presence of a base such as K_2CO_3, Na_2CO_3, NaH or mixtures thereof. The reaction temperature may range from 20 °C to 150 °C, preferably at a temperature in the range from 30 °C to 100 °C. the duration of reaction of the reaction may range from 1 to 24 hours, preferably from 2 to 6 hours.

Alternatively, the novel intermediate of the general formula (1h), can also be prepared by the reaction of compound of general formula (1e),



(1e)



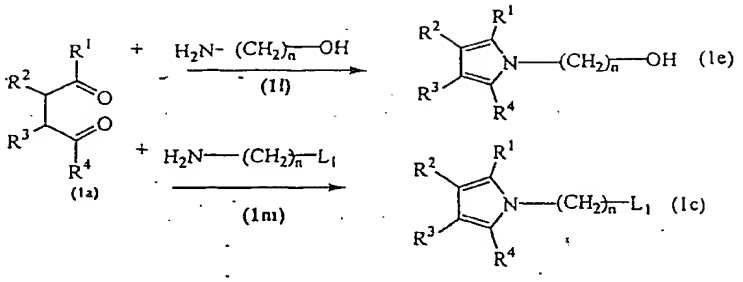
(1k)

wherein $R^1 - R^4$, n are as defined earlier and with a compound of the formula (1k), where Ar is as defined earlier and L^2 is a halogen atom such as fluorine, chlorine, bromine or iodine. The reaction of the compound of formula (1e) with the compound of formula (1k) to produce a compound of formula (1h) may be carried out in the presence of solvents such as THF, DMF, DMSO, DME and the like. Mixture of solvents may be used. The inert atmosphere may be maintained by using inert gases such as N_2, Ar or He. The reaction may be effected in the presence of a base such as K_2CO_3, Na_2CO_3, NaH or mixtures thereof. The reaction temperature may range from 20 °C to 150 °C, preferably at a temperature in the range from 30 °C to 100 °C. The duration of reaction of the reaction may range from 1 to 24 hours, preferably from 2 to 6 hours.

The novel intermediate of the formula (1h) defined above can also be obtained by the reaction of a compound (1e) as defined earlier with the compound of formula (1j) as defined earlier.

The reaction of compound of general formula (1e) with the compound of formula (1j) may be carried out using suitable coupling agents such as dicyclohexyl urea, triarylphosphine/dialkylazadicarboxylate such as PPh_3 /DEAD and the like. The reaction may be carried out in the presence of solvents such as THF, DME, CH_2Cl_2, $CHCl_3$, toluene, acetonitrile, carbontetrachloride and the like. The inert atmosphere may be maintained by using inert gases such as N_2, Ar or He. The reaction may be effected in the presence of DMAP, HOBT and they must be used in the range of 0.05 to 2 equivalents, preferably 0.25 to 1 equivalents. The reaction temperature may range from 0 °C to 100 °C, preferably at a temperature in the range from 20 °C to 80 °C. the duration of reaction of the reaction may range from 0.5 to 24 hours, preferably from 6 to 12 hours.

In another embodiment of this invention, there is provided a process for the preparation of a compound of the general formulae (1c) and (1e), which comprises reacting the compound of general formula (1a)



wherein $R^1 - R^4$ are as defined earlier, with either substituted aminoalcohol (1l), where n is as defined earlier or with substituted amine (1m), where n and L^1 as defined earlier, to yield the intermediate of the general formula (1c) or (1e). The reaction of compound of general formula (1a) with the compound of general formula either (1l) or (1m) may be carried out neat or in presence of solvents or a mixture thereof such as tetrahydrofuran, hexane, toluene, ethanol, heptane, petroleum ether, xylene, benzene, ethyl acetate, tert-butyl acetate, 1,2-dichloroethane, *iso*-propanol, dioxane, cyclohexane and the like. The reaction temperature may range from 0 °C to the reflux temperature of the solvent(s) used. The water produced may be removed by using a Dean Stark water separator or by water scavengers such as molecular sieves. The reaction may be carried out in the presence of an inert atmosphere such as N_2, He or Ar. The reaction may be carried out in the presence of an acid, such as acetic acid, propanoic acid, butyric acid, isobutyric acid, pivalic acid, *p*-toluenesulfonic acid, camphorsulfonic acid, benzenesulfonic acid, trifluoroacetic acid, chloroacetic acid, chloropropanoic acid, phenylacetic acid, phenylpropanoic acid, malonic acid, succinic acid, benzoic acid, halogenated benzoic acid, toluic acid and the like.

The compounds of the present invention contain one or more chiral centers and therefore they also exist as stereoisomers. The stereoisomers of the compounds of the present invention may be prepared by one or more ways presented below:

i. One or more of the reagents may be used in their single isomeric form. For example, compound (1b) or (1d) may be pure stereoisomers.

ii. Optically pure catalysts or chiral ligands along with metal catalysts may be employed in the reduction process. The metal catalyst may be Rhodium, Ruthenium, Indium and the like. The chiral ligands may preferably be chiral phosphines. (Principles of Asymmetric synthesis J E Baldwin Ed. Tetrahedron series, Volume 14, Page no. 311-316)

iii. Mixture of stereoisomers may be resolved by conventional methods such as microbial resolution, resolving the diastereomeric salts formed with chiral acids or chiral bases. Chiral acids may be tartaric acid, mandelic acid, lactic acid, camphorsulfonic acid, amino

acids and the like. Chiral bases may be cinchona alkaloids, brucine or a basic amino acid such as lysine, arginine and the like.

iv. Resolution of the mixture of stereoisomers may also be effected by chemical methods by derivation of the compound with a chiral compound such as chiral amines, chiral acids, chiral amino alcohols, amino acids into a 1:1 mixture of diastereomers and the diastereomers may be separated by conventional methods of fractional crystallization, chromatography and the like followed by cleaving the derivative (Jaques et al. "Enantiomers, Racemates and Resolution", Wiley Interscience, 1981).

The pharmaceutically acceptable salts forming a part of this invention may be prepared by treating the compound of formula (I) with 1-6 equivalents of a base such as sodium hydride, sodium methoxide, sodium ethoxide, sodium hydroxide, potassium tert-butoxide, calcium hydroxide, calcium acetate, calcium chloride, magnesium hydroxide, magnesium chloride and the like. Solvents such as water, acetone, ether, THF, methanol, ethanol, t-butanol, dioxane, isopropanol, isopropyl ether or mixtures thereof may be used. Organic bases such as lysine, arginine, methyl benzylamine, ethanolamine, diethanolamine, tromethamine, choline, guanidine and their derivatives may be used. Acid addition salts, wherever applicable may be prepared by treatment with acids such as tartaric acid, mandelic acid, fumaric acid, maleic acid, lactic acid, salicylic acid, citric acid, ascorbic acid, benzene sulfonic acid, p-toluene sulfonic acid, hydroxynaphthoic acid, methane sulfonic acid, malic acetic acid, benzoic acid, succinic acid, palmitic acid, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid and the like in solvents such as water, alcohols, ethers, ethyl acetate, dioxane, DMF or a lower alkyl ketone such as acetone, or mixtures thereof.

Different polymorphs may by prepared by crystallization of compound of formula (I) under different conditions such as different solvents or solvent mixtures in varying proportions for recrystallization, various ways of crystallization such as slow cooling, fast cooling or a very fast cooling or a gradual cooling during crystallization. Different polymorphs may also be obtained by heating the compound, melting the compound and solidification by gradual or fast cooling, heating or melting under vacuum or under inert atmosphere, and cooling under either vacuum or inert atmosphere. The various polymorphs may be identified by differential scanning calorimeter, powder X-ray diffraction, IR spectroscopy or solid probe NMR spectroscopy.

Another aspect of the present invention comprises a pharmaceutical composition, containing at least one of the compounds of the general formula (I), their derivatives, their

analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates thereof as an active ingredient, together with pharmaceutically employed carriers diluents and the like.

Pharmaceutical compositions containing a compound of the present invention may be prepared by conventional techniques, e.g. as described in Remington: the Science and Practice of Pharmacy, 19th Ed., 1995. The compositions may be in the conventional forms, such as capsules, tablets, powders, solutions, suspensions, syrups, aerosols or topical applications. They may contain suitable solid or liquid carriers or in suitable sterile media to form injectable solutions or suspensions. The compositions may contain 0.5 to 20 %, preferably 0.5 to 10 % by weight of the active compound, the remaining being pharmaceutically acceptable carriers, excipients, diluents, solvents and the like.

Typical compositions containing a compound of formula (I) or a pharmaceutically acceptable acid addition salt thereof, associated with a pharmaceutically acceptable excipients which may be a carrier or a diluent or be diluted by a carrier, or enclosed within a carrier which can be in the form of a capsule, sachet, paper or other container. When the carrier serves as a diluent, it may be solid, semi-solid, or liquid material, which acts as a vehicle, excipients or medium for the active compound. The active compound can be absorbed on a granular solid container for example in a sachet. Some of suitable carriers are water, salt solutions, alcohols, polyethylene glycols, polyhydroxyethoxylated castor oil, peanut oil, olive oil, gelatin, lactose, terra alba, sucrose, cyclodextrin, amylose, magnesium sterate, talc, gelatin, agar, pectin, acacia, stearic acid or lower alkyl ethers of cellulose, silicic acid, fatty acids, fatty acid amines, fatty acids monoglycerides and diglycerides, pentaerythritol fatty acids esters, polyoxyethylene, hydroxymethylcellulose and polyvinylpyrrolidone. Similarly, the carrier or diluent may include any sustained release material known in the art, such as glyceryl monostearate or glyceryl distearate, alone or mixed with a wax. The formulations may also include wetting agents, emulsifying and suspending agents, preserving agents, sweetening agents or flavoring agents. The formulations of the invention may be formulated so as to provide quick, sustained, or delayed release of the active ingredient after administration to the patient by employing procedures well known in the art.

The pharmaceutical compositions can be sterilized and mixed, if desired, with auxiliary agents, emulsifiers, buffers and/or coloring substances and the like, which do not deleteriously react with the active compounds.

The route of administration may be any route, which effectively transports the active drug to the appropriate or desired site of action effectively, such as oral, nasal, transdermal, pulmonary or parental e.g. rectal, depot, subcutaneous, intravenous, intraurethral, intramuscular, intranasal, ophthalmic solution or an ointment, preferably through oral route.

If a solid carrier is used for oral administration, the preparation may be tabletted, placed in a hard gelatin capsule in powder or pellet form or it can be in the form of a troche or lozenge. If a liquid carrier is used, the preparation may be in the form of a syrup, emulsion, soft gelatin capsule or sterile injectable liquid such as an aqueous or non-aqueous liquid suspension or solution.

For nasal administration, the preparation may contain a compound of formula (I) dissolved or suspended in a liquid carrier, in particular an aqueous carrier, for aerosol application. The carrier may contain additives such as solubilizing agent, e.g. propylene glycol, surfactants, absorption enhancers such as lecithin (phosphatidylcholine) or cyclodextrin, or preservatives such as parabens.

For parental application, particularly suitable are injectable solutions or suspensions, preferably aqueous solutions with the active compound dissolved in polyhydroxylated castor oil.

Tablet, dragees or capsules having talc and/or a carbohydrate carrier or binder or the like are particularly suitable for oral application. Preferably, carriers for tablets, dragees or capsules include lactose, corn starch and/or potato starch. A syrup or elixir can be used in cases where a sweetened vehicle can be employed.

A typical tablet which may be prepared by conventional tabletting techniques may contain:

Core:

Active compound (as free compound or salt thereof)	5.0 mg
Colloidal silicon dioxide (Aerosil)	1.5 mg
Cellulose, misrocrytalline (Avicel)	70.0 mg
Modified cellulose gum (Ac-Di-Sol)	7.5 mg
Magnesium sterate	ad.

Coating:

HPMC approx.	9.0 mg
*Mywacett 9-40 T approx	0.9 mg

*Acylated monoglyceride used as plasticizer for film coating.

The compounds of general formula (I) or the compositions thereof are useful for the treatment and/or prophylaxis of disease caused by metabolic disorders such as hyperlipidemia, insulin resistance, Leptin resistance, hyperglycemia, obesity, or inflammation.

These compounds are useful for the treatment of hypercholesteremia, familial hypercholesteremia, hypertriglyceridemia, type 2 diabetes, dyslipidemia, disorders related to syndrome X such as hypertension, obesity, insulin resistance, coronary heart disease, atherosclerosis, xanthoma, stroke, peripheral vascular diseases and related disorders, diabetic complications, certain renal diseases such as glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, psoriasis, polycystic ovarian syndrome, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, arteriosclerosis, Xanthoma, pancreatitis and for the treatment of cancer.

The compounds of the invention may be administered to a mammal, especially, a human in need of such treatment, prevention, elimination, alleviation or amelioration of diseases mentioned above.

The compounds of the present invention are effective over a wide dosage range, however, the exact dosage, mode of administration and form of composition depends upon the subject to be treated and is determined by the physician or veterinarian responsible for treating the subject. Generally, dosages from about 0.025 to about 200 mg preferably from about 0.1 to about 100 mg, per day may be used. Generally, the unit dosage form comprises about 0.01 to 100 mg of the compound of formula (I), as an active ingredient together with a pharmaceutically acceptable carrier. Usually suitable dosage forms for nasal, oral, transdermal or pulmonary administration comprises from about 0.001 mg to about 100 mg, preferably from 0.01 mg to about 50 mg of the active ingredient mixed with a pharmaceutically acceptable carrier or diluent.

In another aspect of the present invention, method of treatment and/or prevention of the diseases mentioned above are provided.

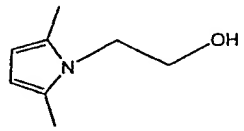
In a further aspect of the present invention, use of one or more compounds of the general formula (I) or pharmaceutically acceptable salts, for the preparation of a medicament thereof for the treatment and/or prevention of diseases mentioned in this document is provided.

In still further aspect of the present invention use of the compounds of the present invention together with statins, glitazones, sulfonylureas, fibric acid derivatives, α-glycosidase inhibitors or antioxidants is provided.

The invention is explained in detail in the examples given below which are provided by the way of illustration only and therefore should not be construed to limit the scope of the invention.

PREPARATION 1:

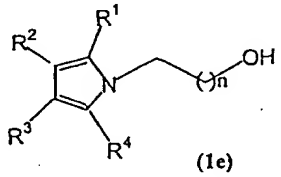
Preparation of 1-(2-hydroxyethyl)-2,5-dimethyl-1*H*-pyrrole (Compound No. 2):



(Compound No. 2)

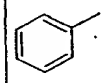
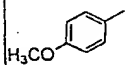
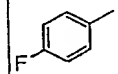
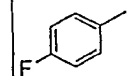
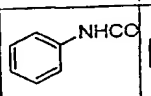
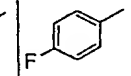
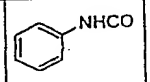
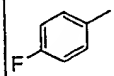
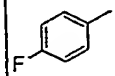
A mixture of hexan-2,5-dione (5 g), ethanolamine (26.7 g), pivalic acid (23.26 g) and the solvent mixture containing n-heptane: tetrahydrofuran: toluene (4:1:1, 5 mL) was refluxed with stirring at 110 – 120 °C. Water formed during the reaction was removed azeotropically during 3 – 4 h. The mixture was cooled and the solvent was removed. The residue obtained was dissolved in dichloromethane (30 mL), washed with saturated sodium bicarbonate solution (30 mL), water (30 mL), and then with brine (30 mL), dried (Na_2SO_4) and the solvent was evaporated. The crude compound obtained as an oily mass, was purified by column chromatography (silica gel 100-200), using ethyl acetate: hexane (2:8) as an eluent to obtain the title compound.

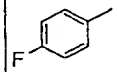
In like manner to that described in Preparation 1, following compounds of the formula (1e) (Given in Table 1) were prepared from the appropriately substituted diketones. The latter can be synthesized by using various routes found in literature.



(1e)

Table 1:

Comp. No.	Substituents on the pyrrole ring in (1e) R^1	R^2	R^3	R^4	n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
1.	H	H	H	H	2	111	98	---
2.	CH_3	H	H	CH_3	2	139	65	2.21 (6H, s); 3.70-3.72 (2H, m); 3.89 (2H, t, J = 5.8 Hz); 5.76 (2H, s).
3.	i-Pr		H	i-Pr	2	271	42	1.25 (12H, 4d, J=6.5 Hz); 2.97 (1H, sept, J = 6.7 Hz); 3.24 (1H, sep, J = 6.7 Hz); 3.85 (2H, m); 4.1 (2H, t, J = 7 Hz); 5.87 (1H, s); 7.19-7.32 (5H, m)
4.	i-Pr	H	H		2	259	84	1.27 (6H, d, J = 6.5 Hz); 2.99-3.04 (1H, m); 3.53 (2H, t, J = 6.15 Hz); 3.82 (3H, s); 4.09 (2H, t, J = 6.2 Hz); 5.96 (1H, d, J = 3.5 Hz); 6.67 (1H, d, J = 3.48 Hz); 6.91 (2H, d, J = 8.9 Hz); 7.29 (2H, d, J = 8.6 Hz)
5.	i-Pr	H	H		2	247	---	1.27 (6H, d, J = 6.0 Hz); 2.97-3.06 (1H, m); 3.53 (2H, t, J = 6.0 Hz); 4.08 (2H, t, J = 6.0 Hz); 5.99 (1H, d, J = 3.60 Hz); 6.10 (1H, d, J = 3.3 Hz); 7.05-7.1 (2H, t, J = 8.8 Hz); 7.34-7.37 (2H, m)
6.	i-Pr	H			2	323.2 (109°C)	55	1.34 (6H, d, J = 7 Hz); 3.09 (1H, sep, J = 7 Hz); 3.57 (2H, t, J = 4.5 Hz); 4.02 (2H, t, J = 4.5 Hz); 7.03-7.30 (9H, m)
7.	i-Pr				2	442 (175 – 178°C)	52	1.47 (6H, d, J = 7.2 Hz); 3.5 – 3.6 (1H, m); 3.59 (2H, t, J = 6.2 Hz); 3.99 (2H, t, J = 6.6 Hz); 6.79 (1H, s); 6.91 – 7.0 (3H, m) 7.08 – 7.19 (10H, m).
8.	i-Pr				3	456 (58 - 62°C)	50	---
9.		-H	H		2	281	79	1.55 (1H, s); 3.3 (2H, dd, J =6.0 Hz); 4.2 (2H, t, J = 6.0 Hz); 6.25 (2H, dd, J =3.6 Hz); 7.1(2H, t, J =7.0 Hz); 7.4 (1H, m, J = 9.0 Hz); 7.42 – 7.47 (6H, m)

Comp. No.	Substituents on the pyrrole ring in (1e)				N =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
10.		-COOEt	H		2	353	55	1.10 (3H, t, J = 7.0 Hz); 1.60 (1H, s, OH); 3.35 (2H, t, J = 6.0 Hz); 4.00 (2H, t, J = 6.0 Hz); 4.10 (2H, t, J = Hz); 6.69 (1H, s); 7.10 (2H, t, J = 9.9 Hz); 7.39 – 7.46 (7H, m)
11.	i-Pr	H	H	CH_3	2	167	68	1.2 (6H, d, J = 8 Hz); 2.2 (3H, s); 2.94 (1H, septet); 3.77 (2H, t, J = 6.9 Hz); 3.97 (2H, t, J = 6.9 Hz)

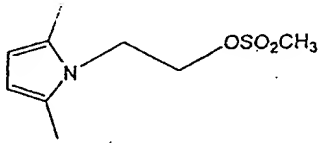
PREPARATION 2 :

Compound 8 described in the table 1, can also be prepared by alternative route using the corresponding aldehyde in better yields. The process is given below:

A mixture containing corresponding aldehyde (2g) and sodium borohydride (0.167 g) was dissolved in absolute alcohol (20 mL). It was stirred at 0-5 °C for about 2 h. The solid product obtained, was diluted with ice-cold water (40 mL), and stirred for 15 min, filtered and washed with water (2 x 10 mL), dried in vacuum desiccator over phosphorous pentoxide (2 g, 100 %).

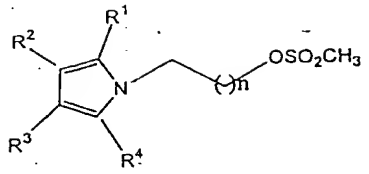
PREPARATION 3:

Preparation of Methyl 2-(2,5-dimethyl-1*H*-pyrrol–1-yl)ethyl sulfonate (Compound No. 13):



To a solution of compound 2 obtained in preparation 1 (3.0 g), triethylamine (11mL) was added methane sulfonyl chloride (5 g) at 0 °C and was stirred at 0 °C for 1h under nitrogen atmosphere. The mixture was warmed to temperature of about 20 to 25 °C and was stirred at that temperature for about 2 h (TLC). After the completion of reaction, water (30 mL) was added and the organic layer was separated. The mixture was washed with saturated sodium bicarbonate solution (20 mL), water (20 mL), and then with brine (20 mL), and dried over Na_2SO_4. The organic layer was evaporated under reduced pressure. The crude substance was used in the next step without purification. In like manner to that described in Preparation 3 following compounds of the formula (1c) (given in Table 2) were prepared from the appropriately substituted pyrrole derivatives (1a) described in Table 1:

Table 2 :



(1c)

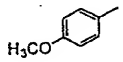
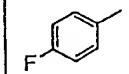
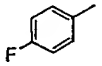
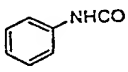
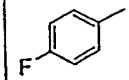
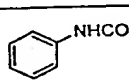
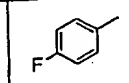
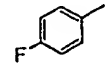
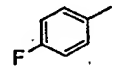
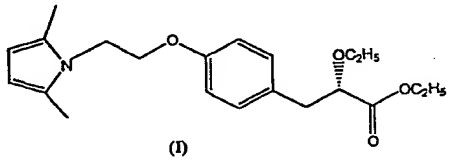
Comp. No.	Substituents on the pyrrole ring in (1c)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
12.	H	H	H	H	2	189	26	2.7 (3H, s); 4.43 (2H, t, J = 5.2 Hz); 6.17 (2H, t, J = 2.1Hz); 6.7 (2H, t, J = 2.1 Hz);
13.	CH_3	H	H	CH_3	2	217	64	2.23 (6H, s); 2.68 (3H, s); 4.08 (2H, t, J = 5.8 Hz); 4.34 (2H, t, J = 5.8 Hz); 5.78 (2H, s)
14.	i-Pr		H	i-Pr	2	349	97	---
15.	i-Pr	H	H		2	337	99	---
16.	i-Pr	H	H		2	325	72	1.29 (6H, d, J = 6.0 Hz); 2.69 (3H, s); 2.92 – 2.99 (1H, m); 4.05 (2H, t, J = 6.0 Hz) 4.27 (2H, t, J = 6.0 Hz); 6.00 (1H, d, J = 3.4 Hz); 6.1 (1H, d, J = 3.4 Hz); 7.07 –7.1 (2H, t, J = 6.0 Hz); 7.30 – 7.35 (2H, m)
17.	i-Pr	H			2	369	61	1.35 (6H, d, J = 7 Hz); 2.76 (3H, s); 3.0 – 3.05 (1H, m); 4.05 (2H, t, J = 6.2 Hz): 4.15 (2H, t, J = 6 Hz); 6.22 (1H, s); 7.07 – 7.30 (9H, m)
18.	i-Pr				2	520 (160 – 162 °C)	85	---
19.	i-Pr				3	534	100	---
20.		H	H		2	359	98	---

Table 2: contd.

Comp. No.	Substituents on the pyrrole ring in (1c)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
21.		-COOEt	H		2	431	98.3	---
22.	i-Pr	H	H	CH_3	2	245	97.1	1.28 (6h, d, J = 7.7 Hz); 2.25 (3H, s); 2.83 – 2.92 (1H, m); 4.14 (2H, t, J = 6.9 Hz); 4.34 (2H, t, J = 6.9 Hz); 5.83 (2H, s).

EXAMPLE 2 :

Preparation of Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate



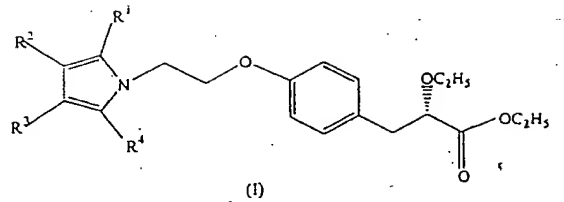
(I)

A mixture ethyl 3-(4-hydroxyphenyl)-2-ethoxypropanoate (1.12 g), and potassium carbonate (2.37 g) in dimethyl formamide (20 mL) was stirred at 70 °C - 80 °C for 10 min, after which mesylate (comp. No.13) (2.3 g) in dimethyl formamide (10 mL) was added. The reaction mixture was stirred at 70 °C to 80 °C for 5 h and allowed to stand overnight at 25 °C – 30 °C (ca.16 h). The reaction mixture was diluted with water (40 mL). The product was extracted with ethyl acetate (2 x 100 mL). The organic layer was washed with saturated sodium bicarbonate solution (65 mL), water (2 x 80 mL), brine (80 mL) and was dried over sodium sulfate. Ethyl acetate was evaporated under reduced pressure to obtain an oily product.

The crude (3 g) product was chromatographed over silica gel using chloroform : ethyl acetate (9 : 1) as an eluent to afford the pure titled compound (2.6 g, 89 %).

In like manner to that described in above example, the following compounds of the formula (I) (given in the Table 3) were prepared from appropriately substituted pyrrole derivatives as described in Table 2:

Table 3 :



(I)

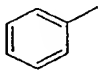
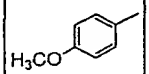
Ex.. No.	Substituents on the pyrrole ring in (I)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
1.	H	H	H	H	2	331	37	1.15 (3H, t, J = 6.9 Hz); 1.22 (3H, t, J = 6.9 Hz); 2.94 (2H, dd); 3.33 – 3.38 (1H, m); 3.54 – 3.65 (1H, m); 3.95 (1H, dd); 4.12 – 4.26 (6H, m); 6.16 (2H, t, J = 2.1Hz); 6.7 (2H, t, J = 2.1Hz); 6.8 (2H, d, J = 8.5Hz); 7.15 (2H, d, J = 8.5Hz).
2	CH_3	H	H	CH_3	2	359	57	1.15 (3H, t, J = 6.9 Hz); 1.25 (3H, t, J = 6.9 Hz); 2.27 (6H, s); 2.91–2.94 (2H, m); 3.32 – 3.60 (2H, m); 3.97 – 4.2 (7H, m); 5.78 (2H, s); 6.78(2H, d, J = 8.5Hz); 7.15 (2H, d, J = 8.5Hz).
3	i-Pr		H	i-Pr	2	491	35	1.16 (3H, t, J = 6.9 Hz); 1.2 –1.3 (15H, m); 2.94 – 2.96 (3H, m); 3.31 – 3.34 (2H, m); 3.96 (2H, t, J = 6.9 Hz); 4.1 – 4.2 (4H, m); 4.3 (2H, t, J = 6.9); 5.89 (1H, s); 6.8 (2H, d, J = 8.5Hz).; 7.15 (2H, d, J = 8.5Hz). 7.2 – 7.33 (5H, m)
4	i-Pr	H	H		2	479	33	1.1 (3H , t, J = 7 Hz); 1.2 (3H , t, J = 7 Hz); 1.31 (6H, d, J= 6 Hz); 3.0 – 3.1 (1H, m); 2.90 (2H, dd); 3.33 (2H, m); 3.8 (3H, s); 3.85 (2H, t,); 3.92 (1H, t); 4.12 – 4.16 (2H, q, J = 7.14 Hz); 4.28 (2H, t, J = 6.8 Hz); 5.98 (1H, d, J = 3.4 Hz); 6.07 (1H, d, J = 3.5 Hz); 6.56 (2H, d, J = 8.6 Hz); 6.93 (2H, d, J = 8.7 Hz) 7.32 (2H, d, J = 8.5 Hz); 7.05 (2H, d, J = 8.5 Hz);

Table 3 : ...contd.

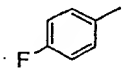
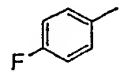
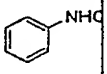
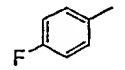
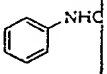
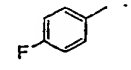
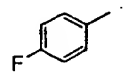
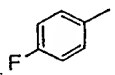
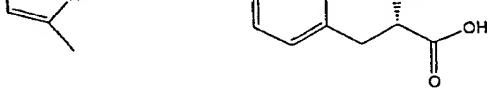
Ex. No.	Substituents on the pyrrole ring in (I)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
5	i-Pr	H	H		2	467	51	1.15 (3H, t, J=6.9Hz); 1.22 (3H, t, J=7.1 Hz); 1.31 (6H, d, J=6 Hz); 2.90 (2H, dd); 3.33-3.35 (1H, m); 3.84 (2H, t, J=6.6 Hz); 3.33 – 3.58 (2H,m); 3.91 - 3.95 (1H, dd); 4.12-4.19(2H, q, J= 7.0 Hz); 4.29 (2H, t, J=6.6 Hz); 6.55 (2H, d, J=8.6 Hz); 6.10 (1H, d, J=3.5 Hz); 5.98 (1H, d, J=3.4 Hz); 7.0 – 7.1 (4H, m); 7.3 – 7.38 (2H, m)
6	i-Pr	H			2	543	48	1.1 (3H, t, J = 6.99 Hz); 1.2 (3H, t, J = 7.1 Hz); 1.36 (6H, d, J = 7 Hz); 2.9 (2H, d, J= 6.29 Hz); 3.0 - 3.1 (1H, m); 3.3 – 3.58 (2H, m); 3.8 (2H, t, J = 6.8 Hz); 3.9 (2H, t, J = 7 Hz); 4.1 – 4.2 (4H, m); 6.2 (1H,s); 6.5 – 7.3 (13H, m).
7	i-Pr				2	662	44	1.08 (3H, t, J = 7.0 Hz); 1.16 (3H, t, J = 7.0 Hz); 1.49 (6H d, J = 7 Hz); 2.85 (2H, dd) 3.26 (1H, m); 3.5 (2H. m) , 3.87 (2H, t); 3.9 (1H, t); 4.09 (2H, q); 4.19 (2H, t); 6.53 (2H, d, J = 8.5 Hz) 6.79 (1H, s); 6.90 – 7.18 (16H, m)
8	i-Pr				3	676	89	1.14 (2H, t, , J = 6.9 Hz) 1.22 (3H, t, J = 7 Hz); 1.53 (6H, d, J = 7 Hz); 1.97 (2H, m); 2.91 (2H,dd) 3.32 (1H, m); 3.56 (2H, m); 3.76 (2H, t); 3.93 (1H, t); 4.07 (2H, t); 4.15 (2H, q, J = 7 Hz); 6.62 – 6.65 (2H, d); 6.84 (1H, s); 6.9 – 6.98 (3H, m) ; 7.03 – 7.05 (2H, d); 7.09 – 7.18 (10H, m).
9		H	H		2	501	15	1.12 (3H, t, J = 7.0 Hz); 1.21 (3H, t, J = 7.0 Hz); 2.88 (2H, d, J = 6.0 Hz); 3.3 (1H, m); 3.6 (1H, m); 3.61 (2H, t); 3.9 (1H, m); 4.1 (2H, t, J = 7.9 Hz); 4.37 (2H, t, J = 6.0 Hz); 6.26 (2H, dd, J =3.3 Hz); 6.9 (2H, d, J = 9.0 Hz); 7.1 (2H, m); 7.41 - 7.49 (9H, m).

Table 3 : ...contd.

Ex. No.	Substituents on the pyrrole ring in (I)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
10		-COOEt	H		2	573	13.5	1.1 - 1.25 (9H, m); 2.8 (2H, d, J = 6.3 Hz); 3.3 (1H, m); 3.6 (1H, m); 3.61 (2H, m); 3.9 (1H, t); 4.1 - 4.21 (6H, m); 6.3 (1H, s); 6.9 (2H, d, J = 9.0 Hz); 7.1 (2H, m); 7.42 - 7.47 (9H, m)
11	i-Pr	H	H	CH_3	2	387	32.4	1.15 (3H, t, J = 6.9 Hz); 1.2 (3H, t, J = 6.9 Hz); 1.25 (6H, d, J = 6.7 Hz); 2.27 (3H,s); 2.9 – 3.0 (3H,m); 3.3 – 3.63 (2H, m); 3.96 (1H, dd,); 4.06 (2H, t, J = 6.9 Hz); 4.14 – 4.24 (4H, m); 5.83 (2H, s); 6.73 (2H, d, J = 8.5 Hz); 7.15 (2H, d, J = 8.5 Hz).

EXAMPLE 13 :

Preparation of 3-{4-[2-(2,5-Dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid

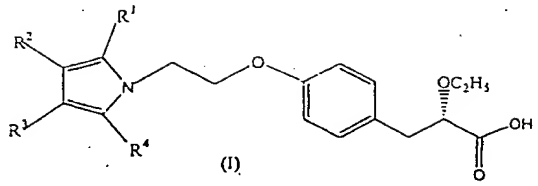


Example no. 13

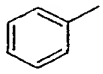
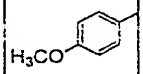
A mixture of substituted ester (prepared in example 2) (1.38 g), sodium hydroxide (3.0 %, 15 mL) in methanol (20 mL) was stirred at 20 °C to 25 °C for 10 h. Methanol was evaporated under reduced pressure. The residue was diluted with water (20 mL) and it was acidified with dilute hydrochloric acid. The product was extracted with ethyl acetate (3 x 20 mL). The organic layer was washed with saturated sodium bicarbonate solution (65 mL), water (2 x 80 mL), brine (80 mL) and it was dried over sodium sulfate to obtain an oily product (1.2 g, 94 %).The crude product (3 g) was separated by column chromatography using silica gel using hexane : ethyl acetate (9 : 1) as an eluent to afford the pure titled compound (0.75 g, 59 %).

In like manner to that described in Example 13 the following compounds of the formula (I) (given in Table 4) were similarly prepared from the appropriately substituted pyrrole derivatives:

Table 4 :

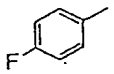
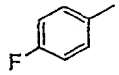
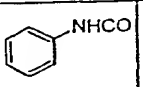
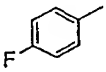
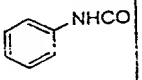
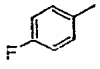
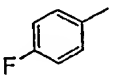


(I)

Ex. No.	Substituents on the pyrrole ring in (I)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
12	H	H	H	H	2	303	79	1.16 (3H, t, J = 6.9Hz); 2.97(1H, dd); 3.0 (1h, dd); 3.36 –3.6 (2H, m); 4.01 (1H, dd); 4.17 – 4.28 (4H, m) 6.16 (2H, t, J = 2.1Hz); 6.75 - 6.80 (4H, m); 6.7 (2H, t, J = 2.1Hz); 6.8 (2H, d, J = 8.5Hz); 7.15 (2H, d, J = 8.5Hz).
13	CH_3	H	H	CH_3	2	331.2 (102)	59	1.18 (3H, t, J = 7 Hz); 2.28 (6H, s); 2.93 - 3.08 (2H, m); 3.45 - 3.59 (2H, m); 4.03 - 4.18 (5H, m); 5.79 (1H, s); 6.78(2H, d, J = 8.5Hz); 7.15 (2H, d, J = 8.5Hz).
14	i-Pr		H	i-Pr	2	463	48	1.12 (3H, t, J = 6.9 Hz); 1.2-1.3 (12H, m); 2.96 - 3.76 (7H, m); 4.03 - 4.05 (2H,m); 4.30 (2H, t, J = 6.9 Hz); 5.89 (1H, s); 6.80 (2H, d, J = 8.5Hz); 7.15 (2H, d, J = 8.5Hz); 7.2 – 7.33 (5H, m).
15	i-Pr	H	H		2	451	84	1.2 (3H, t, J = 7 Hz); 1.29 (6H, d, J = 6 Hz); 2.90 (2H, dd); 3.04 - 3.06 (1H, m); 3.53 – 3.59 (2H, m); 3.8 (3H, s); 4.0 (1H, t); 3.84 (2H, t, J = 6 Hz); 4.28 (2H, t, J = 6. 7 Hz); 5.98 (1H, d, J = 3.4 Hz); 6.56 (2H, d, J = 8.6 Hz); 6.08 (1H, d, J = 3.5 Hz); 6.93 (2H, d, J = 8.7Hz); 7.03 (2H, t, J = 8.5Hz); 7.32 (2H, d, J = 8.5Hz).

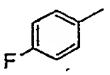
....contd

Table 4 : ....contd.

Ex. No.	Substituents on the pyrrole ring in (I)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
16	i-Pr	H	H		2	439	36	1.17 (3H, t, J = 6.9 Hz); 1.31 (6H, d, J = 6.9 Hz): 2.93 (2H, dd); 3.03 - 3.1 (1H, m); 3.33 - 3.58 (2H, m); 3.84 (2H, t, J = 6.5 Hz); 4.0 (1H, m); 4.29 (2H, t, J = 6.6 Hz); 6.56 (2H, d, J = 8.6 Hz): 6.10 (1H, d, J=3.5 Hz); 6.00 (1H, d, J = 3.5 Hz); 7.0 - 7.1 (4H, m); 7.3 - 7.38 (2H, m).
17	i-Pr	H			2	515 (127-128)	53	1.19 (3H, t, J= 6.9 Hz); 1.36 (6H, d, J=7 Hz); 2.95 (2H, dd, J= 7.1 Hz): 3.0 - 3.1 (1H, m); 3.45 - 3.57 (2H, m); 3.83 (2H, t, J= 6.5 Hz); 4.0 - 4.04 (1H, m); 4.2 (2H, t, J= 6.7 Hz); 6.2 (1H, s); 6.5 –7.28 (13H, m).
18	i-Pr				2	634 (112-114)	61	0.91 (3H, t, J = 6.7 Hz); 1.45 (6H, d, J= 6.8 Hz); 2.91 (2H, dd); 3.13 (1H, m); 3.32 - 3.49 (2H, m); 3.80 (3H; m) 4.15 (2H, t, J= 6.5 Hz); 6.46 (2H, d); 6.78 (1H. s); 6.86 – 7.18 (16H, m).
19	i-Pr				3	648 (114-116)	24	1.1 (3H, t, J=7Hz); 1.47 (6H, d, J=7Hz); 1.91 (2H, m); 3.01 (2H, dd); 3.41 (1H, m); 3.98 (1H, t); 3.71 (2H, t, J= 6 Hz); 4.02 (2H, t, J= 7.2 Hz): 6.59 (1H, t); 6.78 (1H, s); 6.9 (2H, m); 7.1 (10H, m).
20		-H	H		2	473	60.3	0.9 (3H, t); 2.6 (1H, t); 2.9 (2H, d); 3.2 (1H, m); 3.5 (2H, t); 3.6 (1H, m); 6.21 (2H, dd, J= 3 Hz); 6.9 (2H, d); 7.0 (2H, t, J = 9.0 Hz); 7.31 – 7.6 (9H, m).

...contd.

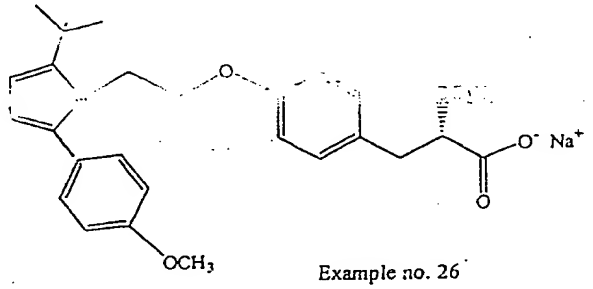
Table 4 : ....contd.

Ex. No.	Substituents on the pyrroie ring in (I)				n =	Mol. Wt. (mp°C)	Yield (%w/w)	^{1}H NMR (300 MHz, δ, $CDCl_3$)
	R^1	R^2	R^3	R^4				
21		-COOEt	H		2	545	83	0.9 (3H, t); 2.6 (1H, t); 2.9 (2H, d); 3.2 (1H, m); 3.5 (2H, t); 3.6 (1H, m); 6.7 (1H, s); 6.9 (2H, d); 7.1 (2H, t); 7.29 – 7.6 (9H, m).
22	i-Pr	H	H	CH_3	2	359	20	1.17 (3H, t, J = 6.9 Hz); 1.26 (6H, d, J = 6.7 Hz); 2.27 (3H,s); 2.9 – 3.0 (1H, m); 3.07 (1H, dd); 3.42 – 3.58 (2H, m); 4.02- 4.08 (3H, m); 4.2 (2H, t, J = 6.3 Hz); 5.83 (2H, s); 6.7 (2H, d, J = 8 Hz); 7.15 (2H, d, J = 8 Hz).

EXAMPLES 23- 33 are the corresponding sodium salts of the acids in the example 12 – 22 prepared according to the following method.

EXAMPLE 26 :

Preparation of sodium salt of 3-{4-[2-(2,5-Dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid



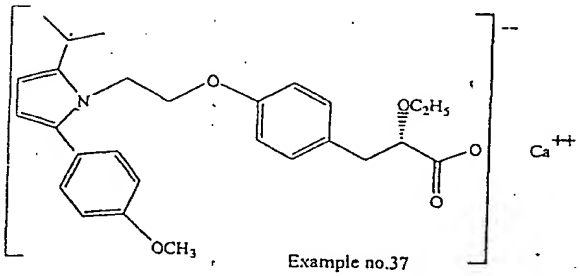
Example no. 26

To acid compound (prepared in example 15 above) (0.64 g) taken in 20 mL methanol, sodium hydroxide (0.056 g) was added and stirred for 3 hour at 20 °C–25 °C. Afterwards, methanol was distilled at reduced pressure, to obtain the titled compound (0.5 g).

EXAMPLES 34- 44 are the corresponding calcium salts of the acids in the example 12 – 22 prepared according to the following method.

EXAMPLE 37 :

Preparation of calcium salt of 3-{4-[2-(2,5-Dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid



Example no.37

The sodium salt (obtained in example 26)(0.5 g) was dissolved in methanol (20 mL) and treated with calcium acetate (0.195 g) at 20 °C – 25 °C. Further, 50 mL of water was added when the calcium salt of the acid precipitates out. The precipitate was filtered, washed with water and then with di-isopropyl ether (2 x 20 mL) to afford the title compound.

Similarly, other pharmaceutically acceptable salts can be prepared in a similar way as described above using the appropriate acids/bases or according to the methods known in literature.

The compounds of the present invention lowered random blood sugar level, triglyceride, total cholesterol, LDL, VLDL and increased HDL. This was demonstrated by in vivo animal experiments.

Demonstration of *in vivo* efficacy of compounds:

1. Plasma triglyceride and total cholesterol lowering activity in Swiss albino mice :

Male Swiss albino mice (SAM) were obtained from NIN, Hyderabad, India and housed in Zydus animal house. All these animals were maintained under 12 hour light and dark cycle at 25±1 °C. Animals were given standard laboratory chow (NIN, Hyderabad, India) and water ad libitum. SAM of 20-25 g body weight range were used.

The test compounds were administered orally to Swiss albino mice at 0.3 to 50 mg / kg/ day dose for 6 days. Control mice were treated with vehicle (0.25% of Carboxymethylcellulose; dose 10 ml/kg).

The blood samples were collected in fed state 1hour after drug administration on 0 and 6 day of the treatment. The blood was collected from the retro-orbital sinus through heparinised capillary and the serum was analyzed for triglyceride and total cholesterol (Wieland, O. Methods of Enzymatic analysis. Bergermeyer, H., O., Ed., 1963. 211-214; Trinder, P. Ann.

Clin. Biochem. 1969. 6: 24-27). Measurement of plasma triglyceride and total cholesterol done using commercial kits (Zydus-Cadila, Pathline, Ahmedabad, India).

Formula for calculation

Percentage reduction in triglycerides/total cholesterol were calculated according to the formula :

$$\text{Percentage reduction (\%)} = 1 - \frac{\left[\frac{TT}{TO}\right]}{\frac{TT}{TC/OC}} \times 100$$

OC = Zero day control group value OT = Zero day treated group value

TC = Test day control group TT = Test day treated group

2. Cholesterol lowering activity in hypercholesterolemic rat models

Male Sprague Dawley rats stock bred in Zydus animal house were maintained under 12 hour light and dark cycle at 25±1 °C. Rats of 180-200 g body weight range were used for the experiment. Animals were made hypercholesterolemic by feeding 2% cholesterol and 1% sodium cholate mixed with standard laboratory chow (NIN, Hyderabad, India) and water ad libitum for 15 days. Throughout the experiment, the animals were maintained on the same diet (Petit, D., Bonnefis, M. T., Rey, C and Infante, R. Effects of ciprofibrate on liver lipids and lipoprotein synthesis in normal and hyperlipidemic rats. Atherosclerosis. 1988. 74: 215-225).

The test compounds were administered orally at a dose 0.1 to 50 mg/ kg/ day for 6 days. Control group was treated with vehicle alone (0.25% of Carboxymethylcellulose; dose 10 ml/kg).

The blood samples were collected in fed state 1hour after drug administration on 0 and 6 day of the treatment. The blood was collected from the retro-orbital sinus through heparinised capillary and the serum samples were analyzed for triglyceride and total cholesterol and HDL using commercial kits (Zydus-Cadila, Pathline, Ahmedabad, India). LDL and VLDL cholesterol were calculated from the data obtained for total cholesterol, HDL and triglyceride. The reductions of various parameters examined are calculated according to the formula.

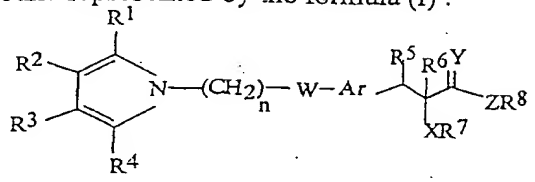
LDL and VLDL cholesterol levels were calculated according to the formula :

LDL cholesterol in mg/dl = Total cholesterol – HDL cholesterol - triglyceride

VLDL cholesterol in mg/dl = Total cholesterol – HDL cholesterol - LDL cholesterol

Claims:

1. A compound represented by the formula (I) :



(I)

its derivatives, its analogs, its tautomeric forms, its stereoisomers, its polymorphs, its pharmaceutically acceptable salts and its pharmaceutically acceptable solvates, wherein one or more groups R^1, R^2 R^3, R^4 may be same or different and represent hydrogen, halogen, perhaloalkyl, hydroxy, thio, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12})alkyl, (C_2-C_{12})alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C_1-C_{12})alkoxy, cyclo(C_3-C_7)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocycloalkoxycarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acid and its derivatives, phosphonic acid and its derivatives; or the adjacent groups R^2 and R^3 together may form a five or a six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from O, N, or S; n is an integer ranging from 1 to 8; W represents O, S or NR^9 where R^9 represents alkyl or aryl; Ar represents a substituted or unsubstituted divalent single or fused aromatic, heteroaromatic or heterocyclic group; R^5 and R^6 represent both hydrogen or together represent a bond; R^5 and R^6 may also represent a hydroxy, alkyl, alkoxy, halogen, acyl, substituted or unsubstituted aralkyl group; X represents O or S; R^7 represents hydrogen, perfluoroalkyl, substituted or unsubstituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, alkoxyalkyl, aryloxyalkyl, alkoxycarbonyl, aryloxycarbonyl, cycloalkyloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl groups; Y represents O or S; Z represents oxygen or NR^{10}, where R^{10} represents hydrogen or substituted or unsubstituted groups selected from alkyl, aryl, aralkyl, hydroxyalkyl, aminoalkyl, heteroaryl,

heteroaralkyl groups; R^8 represents hydrogen, substituted or unsubstituted groups selected from alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, alkoxyalkyl, alkylaminoalkyl groups; R^{10} and R^8 together may form a 5 or 6 membered substituted or unsubstituted cyclic ring structure containing carbon atoms or containing one or more heteroatoms selected from O, N and S.

2. A compound according to claim 1, wherein the substituents on R^1, R^2, R^3 and R^4 are selected from halogen, hydroxy, nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, aralkoxy, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives or phosphonic acid or its derivatives.

3. A compound according to claims 1 and 2, wherein Ar represents substituted or unsubstituted divalent phenylene, naphthylene, benzofuryl, indolyl, indolinyl, quinolinyl, azaindolyl, azaindolinyl, benzothiazolyl or benzoxazolyl groups.

4. A compound according to claim 3, wherein the substituents on the group represented by Ar represents substituted or unsubstituted linear or branched alkyl, alkoxy, halogen, haloalkyl, haloalkoxy, acyl, amino, acylamino, thio or carboxylic or sulfonic acids and their derivatives, phosphonic acid and their derivatives.

5. A compound according to claim 1 which is selected from :

(±) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(+) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(-) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(±) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(+) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(-) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(±) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(+) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(-) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxyropanoate

(±) Ethyl 3-[4-[2-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl-2-ethoxypropanoate

(+) Ethyl 3-[4-[2-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl-2-ethoxypropanoate

(-) Ethyl 3-[4-[2-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl-2-ethoxypropanoate

(±) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(-) Ethyl 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)- 2-ethoxypropanoate

(±) Ethyl 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl)- 2-ethoxypropanoate

(+) Ethyl 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl)-2-ethoxypropanoate

(-) Ethyl 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl)-2-ethoxypropanoate

(±) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanate

(+) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanate

(-) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanate

(±) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(pyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(2,5-dimethylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+)Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(2,5-diisopropyl-3-phenylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-isopropyl-5-(4-methoxyphenyl)pyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-(2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-(2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-(2-[2-(4-fluorophenyl)-5-isopropyl-3-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) 3-(4-(2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy)phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(+) 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-(4-fluorophenyl)-5-phenylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid and its pharmaceutically acceptable salts

(±) Ethyl 3-[4-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl]- 2-ethoxypropanoic and its pharmaceutically acceptable salts

(+) Ethyl 3-[4-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl]- 2-ethoxypropanoic and its pharmaceutically acceptable salts

(-) Ethyl 3-[4-[2-(2-phenyl-3-carboxy-5-(4-fluorophenyl)pyrrol-1-yl)ethoxy]phenyl]- 2-ethoxypropanoic and its pharmaceutically acceptable salts

(±) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salt thereof

(+) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(-) 3-(4-{2-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]ethoxy}phenyl)-2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(±) 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl) -2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(+) 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl) -2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts

(-) 3-(4-{3-[2-(4-fluorophenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoylpyrrol-1-yl]propoxy}phenyl) -2-ethoxypropanoic acid ethyl ester and its pharmaceutically acceptable salts.

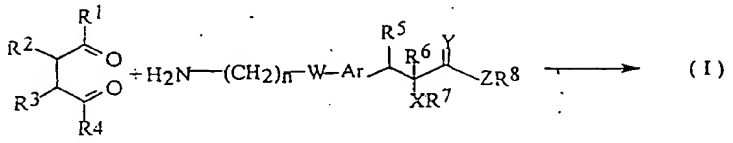
(±) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic and its pharmaceutically acceptable salts

(+) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic and its pharmaceutically acceptable salts

(-) Ethyl 3-{4-[2-(2-isopropyl-5-methylpyrrol-1-yl)ethoxy]phenyl}-2-ethoxypropanoic and its pharmaceutically acceptable salts

6. A process for the preparation of a compound of formula (I) according to claim 1 selected from ;

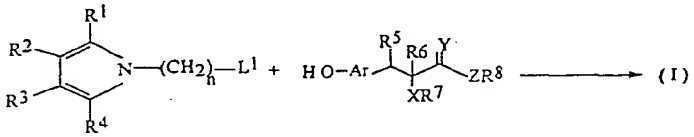
a. reacting a compound of formula (1a),



(1a) (1b) (I)

where all the symbols are as defined earlier, with a compound of formula (1b) which may be racemic or chiral, where all symbols are as defined earlier to yield a compound of formula (I) where all symbols are as defined earlier;

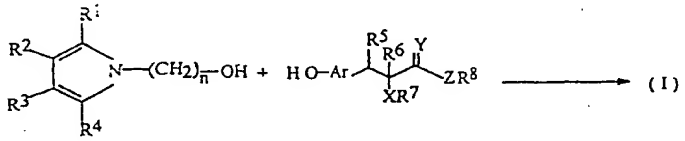
b. reacting a compound of formula (1c),



(1c) (1d) (I)

where all the symbols are as defined earlier and L^1 represents a leaving group, with a compound of formula (1d) which may be racemic or chiral, wherein all symbols are as defined earlier;

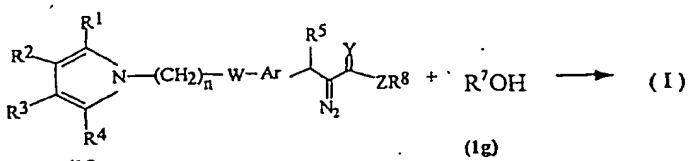
c. reacting the compound of formula (1e),



(1e) (1d) (I)

where all symbols are as defined earlier with a compound of general formula (1d) which may be racemic or chiral, defined earlier;

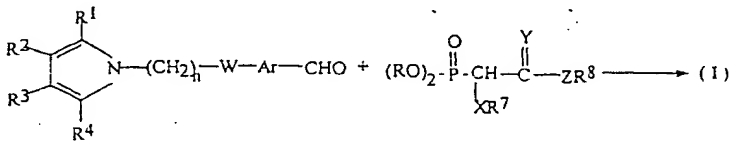
d. reacting a compound of formula (1f)



(1f) (1g) (I)

where all the symbols are as defined earlier with an alcohol of formula (1g) wherein R^7 is as defined earlier except H to produce a compound of formula (I) , to produce a compound of general formula (I) wherein all symbols are as defined earlier and X represents 'O' atoms ;

e. reacting a compound of general formula (1h),



(1h) (1i)

where all the symbols are as defined earlier, with a compound of formula (1i) which may be chiral or racemic, where all the symbols are as defined earlier and R represents (C_1-C_8) alkyl to afford a compound of formula (I) wherein all symbols are as defined earlier and R^5 and R^6 together form a bond;

7. A process according to the claim 6, comprising of carrying out one or more of the following optional steps:

i. Converting a compound of formula (I) into a further compound of formula (I);

ii. Removing any protecting group;

iii. Resolving the racemic mixture into pure enantiomers by the known methods and

iv. Preparing a pharmaceutically acceptable salt of a compound of formula (I) and/or a pharmaceutically acceptable solvate thereof.

8. A compound of the general formula (I), its derivatives, its analogs, its tautomeric forms, its stereoisomers, its polymorphs, its pharmaceutically acceptable salts and its pharmaceutically acceptable solvates for preparing a medicament.

9. A pharmaceutical composition which comprises a compound according to general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them.

10. A pharmaceutical composition which comprises a compound according to general formula (I), according to claim 9, in the form of a tablet, capsule, powder, syrup, solution or suspension.

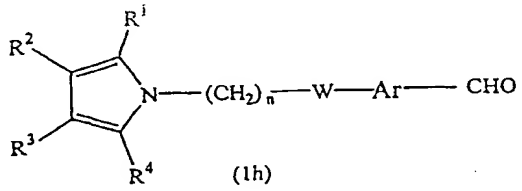
11. Use of a compound of the general formula (I), as defined in claims 1 to 4 or pharmaceutical composition as claimed in claim 9, for use in the treatment of and/or prophylaxis of hyperglycemia, hyperlipidemia, hypertension, cardiovascular disease and certain eating disorders.

12. Use of a compound of formula (I), as defined in claims 1 to 4 or pharmaceutical composition as claimed in claim 9 and 10, for the treatment of and/or prophylaxis of hyperglycemia, hyperlipidemia, hypertension, cardiovascular disease and certain eating disorders in human and non-human which comprises administering an effective, non-toxic, amount of a compound of the general formula (I), its derivatives, its analogs, its tautomeric forms, its stereoisomers, its polymorphs, its pharmaceutically acceptable salts and its pharmaceutically acceptable solvates.

13. Use of a compound of formula (I), as defined in claims 1 to 4 or a pharmaceutical compositions as claimed in claim 9 and 10, for the manufacture of a medicament for the treatment and /or prophylaxis of hyperglycemia, hyperlipidemia, hypertension, cardiovascular disease and certain eating disorders.

14. A method for the treatment of and/or prophylaxis of hyperglycemia, hyperlipidemia, hypertension, cardiovascular disease and certain eating disorders in human and non-human which comprises administering an effective, non-toxic, amount of a compound according to claim 1.

15. Novel intermediate defined by the formula (1h),

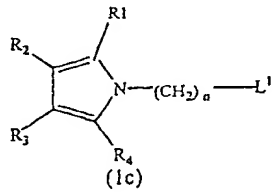


(1h)

wherein one or more groups R^1, R^2 R^3, R^4 may be same or different and represent hydrogen, halogen, perhaloalkyl, hydroxy, thio, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12})alkyl, (C_2-C_{12})alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C_1-C_{12})alkoxy, cyclo(C_3-C_7)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocycloalkoxycarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl,

hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acid and its derivatives, phosphonic acid and its derivatives; or the adjacent groups R^2 and R^3 together may form a five or a six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from O, N, or S; n is an integer ranging from 1 to 8; W represents O, S or NR^9 where R^9 represents alkyl or aryl; Ar represents a substituted or unsubstituted divalent single or fused aromatic, heteroaromatic or heterocyclic group.

16. A novel intermediate of the general formula (1c),

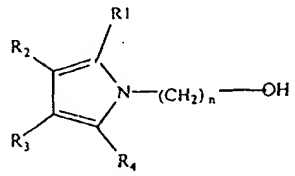


(1c)

wherein one or more groups R^1, R^2 R^3, R^4 may be same or different and represent hydrogen, halogen, perhaloalkyl, hydroxy, thio, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12})alkyl, (C_2-C_{12})alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C_1-C_{12})alkoxy, cyclo(C_3-C_7)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocycloalkoxycarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acid and its derivatives, phosphonic acid and its derivatives; or the adjacent groups R^2 and R^3 together may form a five or a six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from O, N, or S; n is an integer

ranging from 1 to 8; and L^1 is either a halogen atom such as chlorine, bromine or iodine or a leaving group such as methanesulfonate, trifluoromethanesulfonate and p-toluenesulfonate groups.

17. The novel intermediate of the formula (1e)

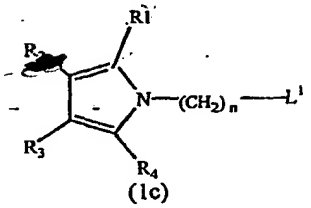


(1e)

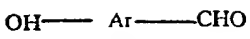
wherein one or more groups R^1, R^2 R^3, R^4 may be same or different and represent hydrogen, halogen, perhaloalkyl, hydroxy, thio, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12})alkyl, (C_2-C_{12})alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C_1-C_{12})alkoxy, cyclo(C_3-C_7)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocycloalkoxycarbonyl, heteroaryloxycarbonyl, heteroaralkoxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acid and its derivatives, phosphonic acid and its derivatives; or the adjacent groups R^2 and R^3 together may form a five or a six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from O, N, or S; n is an integer ranging from 1 to 8.

18. A process provided for the preparation of novel intermediate of the general formula (1h), which comprises,

a. reacting the novel compound of the general formula (1c) as described in claim 16,



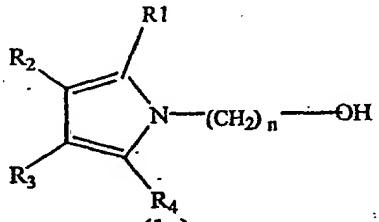
(1c)



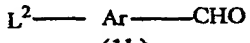
(1j)

with the compound of general formula (1j), where Ar is as defined in claims 1, 3 and 4.

b. reacting the novel compound of the formula (1e) as described in claim 17,



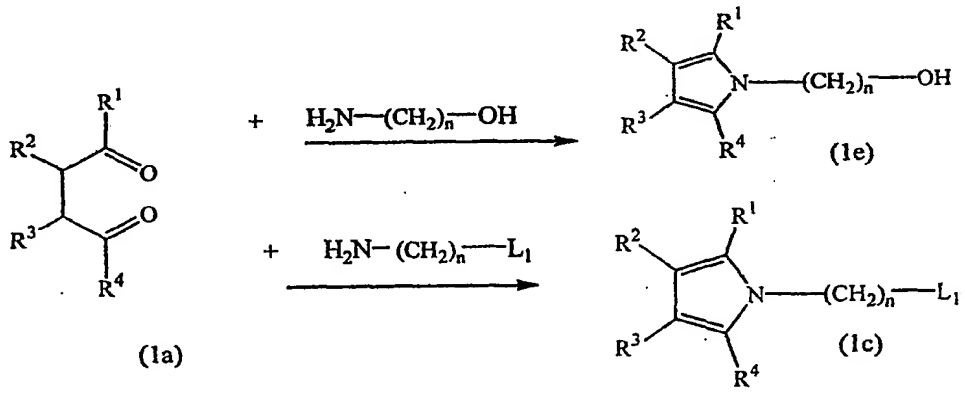
(1e)



(1k)

with compound of the formula (1k), where L^2 is a halogen atom such as fluorine, chlorine, bromine or iodine and Ar is as defined in the claims 1, 3 and 4.

19. A process to prepare the intermediates (1e) or (1c) which comprises,



(1a) (1e) (1c)

reacting the compound of formula (1a) with (1l) and (1m) where all symbols are as defined earlier.